CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

63065

ADMINISTRATIVE DOCUMENTS

January 24, 1989

Chemist, HFD-235

Abbreviated Antibiotic Drug Application #63-065

Director, Anti-Microbial Drug Branch, HFD-473

Danbury Pharmaceutical, Inc. has submitted an Abbreviated Antibiotic Drug Application for Minocycline Hydrochloride Capsules. Please perform the required compendial tests.

The following are being forwarded with his memo:

1. Duplicate copy of the application.
2. Samples with Certificates of analysis for three batches.

If there are any questions, I may be reached at 443-4340.

John M. Singer

~~HFD-235~~
HFD-235/DD
R/D JSinger
HFD-230/Dr. Seife
1/24/89 bcw 5687d

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Memorandum

e March 12, 1990

From Chief, Antimicrobial Drugs Branch
HFD-473

Subject Form 63-065; Minocycline Hydrochloride CapsulesUSP (100 mg);
Danbury Pharmacal, Inc.

To John D. Harrison
HFD-235

This application adequately describes the composition of the subject product. All of the components are to meet the requirements of the official compendia. The bulk antibiotic is obtained from FDA approved sources. Adequate procedures are described for the inventory and quality control of the raw components. The capsules are to be formulated with no deliberate excess of minocycline in batches of 500 M, 1 MM and 2 MM. The manufacturing process and the process controls are adequately described. The required testing of the components and finished capsules is done in-house assisted by four consultant laboratories. A suitable protocol is in place to govern the reworking of any batch found to be out of compliance. The capsules (#2 hard gelatine) are packaged in HDPE bottles, with coil and metal screw caps with liner.

Control numbers are assigned sequentially when Batch Manufacturing Records are made. There is no further description of this system other than each number is suffixed with a "C". The exhibits have lot numbers that appear to fit this description.

Adequate protocols for the conduct of accelerated (37-40°C/75%RH) and long term (CRT) stability studies are submitted. There are no data from these studies in the materials received in ADB.

ADB received exhibits from three batches of this product accompanied by their batch records and certificates of analysis. The records show that: (1) batch 00755C was manufactured on 8/16/'88 and contained M capsules; (2) batches 01218C and 01219C were manufactured on 1/10/89 from the same minocycline HCl bulk and each contained capsules.

ADB examined the exhibits for conformance to CFR and USP requirements when they were approximately 14 to 18 months old. The results for potency and dissolution are satisfactory. The interlaboratory agreement between the potency values is reasonably good. These results are reported in the attached Chemistry Review Notes.

The sizes of parent batches of the exhibit samples do not meet the current guidelines nor do they meet ADB's old unofficial 10% minimum guideline. By the current 15% minimum these batch sizes qualify for a maximum batch size of about M capsules. This is about a half of the smallest production batch that Danbury indicates its intention to

manufacture. At best, a maximum of M capules would be permissable under ADB's old guideline. The application is incomplete on account of its lack of stability data. If satisfactory stability data have been submitted to you, ADB would concur in the approval of this application with the above batch size restriction.

/S/
Joseph H. Graham, Ph.D.

cc: HFD-470 (Overpeck)
HFD-473 (Chem. Sec.; R/F)

JHG/ymb
0138Y

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 10/25/90

NDA NUMBER: 63-065

IND NUMBER:

TELECON/MEETING

INITIATED BY: [X] APPLICANT/SPONSOR [X] FDA

MADE: [X] BY TELEPHONE [ ] IN PERSON

PRODUCT NAME: Minocycline Hydrochloride

FIRM NAME: Danbury

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Bruce Cohen, Reg. Affairs

TELEPHONE NO.: 203-744-7200

1. I called Danbury to tell them that their AADA #63-065 could go forward from my desk once I had received a revised package insert to reflect deletion of the 50 mg capsule from the current insert (due to the fact that the application for the 50 mg potency in much farther down the queue). (The other questions regarding possibly requiring additional changes related to the whole question because of Lederle's "pelletized" minocycline have been laid to rest).

2. Mr. Cohen called me back at 4:00 Friday pm to state that the package insert would be changed to delete reference to the 50 mg strength and that the revised inserts would be hand carried to document control room and here on Monday. He asked me about the prospects for approval - I told him that from my viewpoint, the application would go forward.

SIGNATURE: /S/ Richard C. Adams

DIVISION: Generic Drugs

FORM FD 2587 (11/77)

ORIGINAL IND/NDA

U. S. GOVERNMENT PRINTING OFFICE-1984-432-976/7126

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Memorandum

Date October 18, 1990

From Division of Generic Drugs — HFD- 632

Requestor's Name Richard C. Adams — Phone 295-8370

Subject ESTABLISHMENT EVALUATION REQUEST

To Division of Manufacturing & Product Quality (HFD-320)

Sterile Product _____ Non Sterile Product X

Application and Supplement No. 63-065

Brand Name *(if any)* _____

Establishment Name, Dosage Form and Strength Minocycline Hydrochloride Capsules, 100 mg

_____ Profile Class Code: CHC

Priority Classification: _____ *(See SMG BD-4820.3)*

Applicant's Name: Danbury Pharmacal, Inc.

Address: 12 Stonehigh Avenue, Carmel, New York 10512

Facilities to be Evaluated: (*Name, full Address, DMF No., and responsibility*) — **For HFD 320 Use** Status & Date of Inspection:

1. Applicant _____
2. _____
3. _____
4. _____
5. _____

Other Information or Special Requests: _____

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For HFD-320 Use Only: Date Received: _____

CGMP Compliance Status of Facilities Evaluated: _____

CSO: _____ Date Completed: _____

Distribution: Original and First Copy: HFD-320
Remaining Copies: Requesting Office Use

FORM FDA 3274 (3/90)

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 10/18/90, 10/19/90

NDA NUMBER: 63-065

IND NUMBER:

TELECON/MEETING

INITIATED BY: [X] APPLICANT/SPONSOR [X] FDA

MADE: [ ] BY TELEPHONE [ ] IN PERSON

PRODUCT NAME: Minocycline Hydrochloride

FIRM NAME: Danbury

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD:

Reg. Affairs(?)
VP, Scientific Operations
E.M. Cohen

TELEPHONE NO.: 203-744-7200

1. I called Danbury because the final package insert indicates that minocycline hydrochloride capsules are supplied in both 50 and 100 mg strengths. Danbury has another pending application for Minocycline HCl 50 mg capsules (AADA 63-18[illegible]) but no action will be taken for sometime since it is considerably further down the queue. Also, no expiration date was explicitly stated anywhere in the application. Ms(?) said she would get back to me on Oct. 19.

2. Mr. Cohen called at 8:00AM and put me on conference line. I explained the package insert problem to him and he assured me that a revised package insert and an accompanying amendment would be sent by COB 10/23. He inquired as to the disposition of this AADA following correction of the FPL problem I told him that, as far as I was concerned, the application would be forwarded. (also, he assured me that the expiration dating of 24 months would be explicitly represented).

3. Mr. Cohen called again (9:00AM) 10/19 to mention that 24 month expiration was stated in Amendment #007 (correct) and to confirm deletion of reference to 50 mg capsules in package insert in three places.

SIGNATURE: Richard C. Adams /S/

DIVISION: Generic Drugs Div. II

FORM FD 2587 (11/77)

ORIGINAL IND/NDA

U. S. GOVERNMENT PRINTING OFFICE-1984-432-976/7126

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: November 5, 1990

TO: Labeling Review Branch (HFD-638)

FROM: Antibiotic Drug Review Branch (HFD-635)

SUBJECT: Minocycline Hydrochloride Capsules, Equivalent to 100 mg minocycline
Danbury Pharmacal, Inc. ANDA 63-065 AL

Please review labeling contained in attached submission dated October 29, 1990.

John D. Harrison

Vol. 4.1

DEPARTMENT OF HEALTH & HUMAN SERVICES 2205

Public Health Service

also - Reg ort 1534

~~PRE-AMENDMENT~~ UPDATE

Memorandum

ate November 14, 1991

From Division of Generic Drugs HFD- 632

Requestor's Name Richard Adams/Dave Doleski Phone 295-8305

Subject ESTABLISHMENT EVALUATION REQUEST /S/

To Division of Manufacturing & Product Quality (HFD-320)

Sterile Product _____ Non Sterile Product X

Application and Supplement No. 63-181, 63-065

Brand Name *(if any)* 50mg 100mg

Establishment Name, Dosage Form and Strength Minocycline Hydrochloride Capsules, 50 mg, 100mg

_____ Profile Class Code: CHG

Priority Classification: _____ *(See SMG BD-4820.3)*

Applicant's Name: Danbury Pharmacal, Inc.

Address: 131 West St. - P.O. Box 296 - Danbury, CT 06813

Facilities to be Evaluated: (*Name, full Address, DMF No., and responsibility*)

For HFD 320 Use
Status & Date of Inspection:

1. Danbury Pharmacal, Inc. 12 Stoneleigh Ave. - Carmel, NY — AC 5/7/91
2. _____ — Withdrawn
3. _____ — AC-12/4/90 Stability and Dissolution Te
4. _____ — AC- 8/30/90
5. _____ — _____

Other Information or Special Requests: _____

****

For HFD-320 Use Only: Date Received: 11/21/91

CGMP Compliance Status of Facilities Evaluated: Acceptable

CSO: /S/ Date Completed: 11/27/91

Distribution: Original and First Copy: HFD-320
Remaining Copies: Requesting Office Use

FORM FDA 3274 (3/90)

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE	May 22, 1991
NDA NUMBER	(63-065, 63-181
IND NUMBER	
TELECON/MEETING	INITIATED BY: ☒ APPLICANT/SPONSOR (1) ☐ FDA (1); MADE: ☒ BY TELEPHONE ☐ IN PERSON
PRODUCT NAME	Minocycline: Tablets and capsules
FIRM NAME	Danbury
NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD	E. M. Cohen / L. Gelber, V.P. Reg. affairs
TELEPHONE NO.	914-225-1700

Background:

The two tablet applications, were reviewed by me and, pending receipt of final 6 mo's CRT stability data and favorable EER report, from a chemistry standpoint are approvable. It was decided by Bioequivalence Division, however, that another "small" food study would be required (fasting blood levels vs. "fed" blood levels) and this was recently communicated to the company.

For the two capsule applications the original biostudy was done on the 100 mg. strength and this was prepared from bulk, an as yet unapproved supplier - the basis for a Nov. 8 N/A letter to firm. Therefore Danbury prepared of 100 mg. capsules from bulk and conducted a biostudy and submitted in ~~January~~ April. The 50 mg capsule needs to have comparative dissolution data run against these 100 mg. capsules as the basis for a bio waiver request.

These phone conversations ~~was~~ were held to clarify these issues.

SIGNATURE: /S/

DIVISION: Generic Drugs

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 10/29/91

NDA NUMBER: 63-181
63-065

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☒ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Minocycline Hydrochloride Capsules

FIRM NAME: Dearborn

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: L.J. Cohen

TELEPHONE NO.: 914-225-7700

9:30AM

Per conversation w Tom Sanx & Dick Adams, labeling comments are the only outstanding deficiency. The firm was notified of these labeling changes. The firm will ofr a draft copy to me today and then will submit 12 PL.

SIGNATURE: /S/

DIVISION: OGD

FORM FD 2587 (11/77)

ORIGINATOR

RECORD OF TELEPHONE CONVERSATION/MEETING

Firm called to discuss labeling issues related to these four applications. I suggested that they resolve these issues with labeling reviewer and turned the matter over to Jerry Phillips.

DATE
Oct. 28, 1991

NDA NUMBER
63-065, 181,

IND NUMBER

TELECON/MEETING

INITIATED BY
☒ APPLICANT/ SPONSOR
☐ POA

MADE
☐ BY TELEPHONE
☐ IN PERSON

PRODUCT NAME
Mirtazapine. HCl
Tablets and
Capsules

FIRM NAME
Danbury

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Soren Gelber,
Reg. Affairs.

TELEPHONE NO.
914-225-1700

SIGNATURE
/S/

DIVISION
Generic Drugs

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE: 1991 O-277-703

AMENDMENT REVIEW FOR COMPLETENESS

ANDA/AADA

CHEMIST Adams

ROUTING:

Application Examiner A. L. Date: 5-23-91
CSO Date:
Branch Chief Jay Date: 5/30/91

Attached is an amdendment dated May 17, 1991 received May 21, 1991 submitted in response to a non-approvable (NA) letter dated March 28, 1991 (attached).

Amendment to Supplement _____

Amendment to Original Application AADA 63-065

Is amendment a complete response to deficiency letter?

Application Examiner	CSO	Branch Chief
Yes ✓	Yes ✓	Yes ✓
No _____	No _____	No _____

Is submission a minor amendment (30 days) or major amendment (120 days)?

Application Examiner	CSO	Branch Chief
Minor ✓	Minor ✓	Minor ✓
Major _____	Major _____	Major _____

Note: A Non-Approvable (NA) letter will issue for any amendment (original or supplemental) which is submitted after April 4, 1990, submitted in response to an Agency deficiency letter, and is incomplete in that it does not address all deficiencies stated in the letter.

Determinations of minor and major amendment status will be determined for original application amendments submitted after March 7, 1990 and for supplemental amendments submitted after May 22, 1990.

0248M

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: May 23, 1991

TO: Labeling Review Branch (HFD-638)

FROM: Antibiotic Drug Review Branch (HFD-635)

SUBJECT: Minocycline Hydrochloride capsules
Danbury Pharmaceutical, Inc. NADA 63-065

Please review labeling contained in attached submission dated May 17, 1991

John D. Harrison

REVIEW OF PROFESSIONAL LABELING

Orig. Amendment

DRAFT insert

DATE OF REVIEW: 6/10//91

AADA #: 63-065

NAME OF FIRM: Danbury

NAME OF DRUG: Minocycline Hydrochloride Capsules USP, 100mg

DATE OF SUBMISSION: May 17, 1991

COMMENTS:

Insert: Not Satisfactory

A. DESCRIPTION:

Revise the following:

Each minocycline hydrochloride capsule, for oral administration, contains the equivalent of 50 mg or 100 mg of minocycline. In addition, each capsule contains the following inactive ingredients...

B. CLINICAL PHARMACOLOGY

1. Paragraph 1:

...minocycline hydrochloride capsules or tablets,...

2. Susceptibility Tests (Diffusion Techniques; Paragraph 1)
...microorganisms to minocycline. One such...

C. WARNINGS:

MINOCYCLINE LIKE OTHER TETRACYCLINE-CLASS...

D. PRECAUTIONS (General)

1. Begin paragraph 2 with the third sentence.

2. Begin paragraph 3 with the final sentence.

E. ADVERSE REACTIONS (Renal toxicity)

Elevations in...

F. DOSAGE AND ADMINISTRATION

1. Paragraph 2:

Minocycline hydrochloride capsules or tablets...

2. ADULTS

-Delete

-"hydrochloride" should not begin with a capital letter.

G. HOW SUPPLIED

Delete when describing the dosage form in this section.

H. REFERENCES

Align your references correctly.

RECOMMENDATIONS:

1. Inform the firm of the above comments.

2. Request the firm revise their insert labeling, then prepare and submit twelve final printed copies.

/S/ 6/19/91

Jerry Phillips

cc:
HFD-638/JPhillips/TPoux
HFD-635

REVIEW LABELING

J Mattli for TP 6/19/91

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 11/13/91

NDA NUMBER: 63-181, 63-065

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☒ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Minocycline HCl

FIRM NAME: Danbury

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Loren Gelber, Reg. Affairs.

TELEPHONE NO.: 914-225-1700
914-278-3715 (Direct line to Loren Gelber office)

I called firm because Jerry Phillips said that he was still awaiting FPL from Danbury before he could process these applications. Loren Gelber stated that FPL was hand delivered to OGD on 11/1/91.

I conveyed this to Jerry Phillips and then located the 11/1/91 communications re: labeling and turned it over to Jerry who said he would look at it.

SIGNATURE: /S/

DIVISION: Generic Drugs.

FORM FD 2587 (11/77)

DIVISION FILE

U. S. GOVERNMENT PRINTING OFFICE