

**Correspondence from Applicant**

**09-27-00**



**OPHARMA, INC.**

www.orpharma.com

*Rec'd. 10-10-00  
CCG*



732 Louis Drive  
Warminster, PA 18974

215/956-2200 Tel  
215/443-9531 Fax

September 27, 2000

Jonathan K. Wilkin, MD  
Director, Division of Dermatological and Dental Drug Products (HFD-540)  
Center for Drug Evaluation & Research  
Food and Drug Administration  
Document Control Room  
9201 Corporate Boulevard  
Rockville, MD 20850

RECEIVED

*BB*

RE: NDA 50-781  
Minocycline PTS  
Amendment: Biopharmaceutics Requested Information

Dear Dr. Wilkin:

Reference is made to telefax received on September 20, 2000 requesting additional information for the Biopharmaceutics Reviewer.

This amendment provides information / data to the FDA questions or request. I have listed each point separately followed by our response.

If you have any questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

*Markus F. Herzig*  
Markus F. Herzig

Executive Director, Regulatory Affairs and Quality Assurance

Form FDA 356h  
Submitted in duplicate

ORIGINAL

Question 1

Question 2

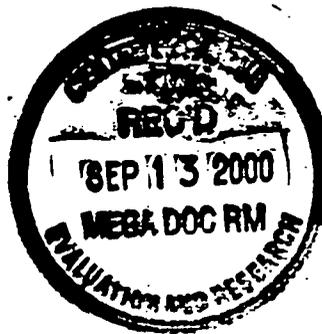
Question 3

Question 4

Attachment 1

**ORAPHARMA INC.**

www.orapharma.com



732 Louis Drive  
Warminster, PA 18974

215/956-2200 Tel  
215/443-9531 Fax

September 11, 2000

Jonathan K. Wilkin, MD  
Director, Division of Dermatological and Dental Drug Products (HFD-540)  
Center for Drug Evaluation & Research  
Food and Drug Administration  
Document Control Room  
9201 Corporate Boulevard  
Rockville, MD 20850

**AMENDMENT**

BC

RE: NDA: 50-781  
Minocycline PTS  
CMC Amendment: FDA / Sponsor Contact Report

Dear Dr. Wilkin:

Attached is the contact report I prepared from the FDA / OraPharma teleconference held on September 5, 2000.

This teleconference was requested by your Chemistry review team to discuss a product identifier for our unit dose dispensers.

If you have any questions regarding this submission, please contact me at (215) 956-2207.

Sincerely,

Markus F. Herzig  
Executive Director, Regulatory Affairs and Quality Assurance

Form FDA 356h  
Submitted in duplicate

**ORIGINAL**

**Correspondence from Applicant**

**08-16-00**



**GRAPHARMA INC.**

www.grapharma.com

732 Louis Drive  
Warminster, PA 18974

215/956-2200 Tel  
215/443-9531 Fax

AMENDMENT

B.C.

August 16, 2000

Jonathan K. Wilkin, MD  
Director, Division of Dermatological and Dental Drug Products (HFD-540)  
Center for Drug Evaluation & Research  
Food and Drug Administration  
Document Control Room  
9201 Corporate Boulevard  
Rockville, MD 20850

RE: NDA 50-781  
ARESTIN (Minocycline HCl) Microspheres  
Amendment: Product Packaging and Pouch with Label

Dear Dr. Wilkin:

As was requested by Ms. Kalyani Bhatt, Project Manager in your Division, enclosed are samples of the product box which will contain two resealable pouches of ARESTIN dispensers. Also provided are samples of the pouches as well as the labels for these pouches. The size of the box is approximately 75% of actual size, whereas the pouches and pouch labels are actual size.

If you have any questions regarding this submission please call me at (215) 956-2207.

Sincerely,

Markus F. Herzig  
Executive Director, Regulatory Affairs

MFH:stk

Attachments

Form FDA 356h

DUPLICATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338  
Expiration Date: April 30, 2000  
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,  
OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT OraPharma, Inc.	DATE OF SUBMISSION: August 16, 2000
TELEPHONE NO. (Include Area Code) 215-956-2200	FACSIMILE (FAX) Number (Include Area Code) 215-443-9531
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 732 Louis Drive Warminster, PA 18974	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Markus F. Herzig 732 Louis Drive Warminster, PA 18974

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued) 50-781

ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Minocycline PTS (Minocycline Periodontal Therapeutic System)	PROPRIETARY NAME (trade name) IF ANY ---	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any) 7 - dimethylamine - 6 - demethyl - 6 - deoxytetracycline hydrochloride	CODE NAME (if any) --	
DOSAGE FORM: topical	STRENGTHS: 1 mg	ROUTE OF ADMINISTRATION: Subgingival

(PROPOSED) INDICATION(S) FOR USE: Adjunctive therapy to scaling and root planing procedures in patients with adult periodontitis

APPLICATION INFORMATION

APPLICATION TYPE (check one)  
 NEW DRUG APPLICATION (21 CFR 314.50)  ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)  
 BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE  505 (b)(1)  505 (b)(2)  507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION  
Name of Drug \_\_\_\_\_ Holder of Approved Application \_\_\_\_\_

TYPE OF SUBMISSION (check one)  
 ORIGINAL APPLICATION  AMENDMENT TO A PENDING APPLICATION  RESUBMISSION  
 PRESUBMISSION  ANNUAL REPORT  ESTABLISHMENT DESCRIPTION SUPPLEMENT  SUPAC SUPPLEMENT  
 EFFICACY SUPPLEMENT  LABELING SUPPLEMENT  CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT  OTHER

REASON FOR SUBMISSION Requested Information

PROPOSED MARKETING STATUS (check one)  PRESCRIPTION PRODUCT (Rx)  OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED \_\_\_\_\_ THIS APPLICATION IS  PAPER  PAPER AND ELECTRONIC  ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary) Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

NA

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

NA

This application contains the following items: (Check all that apply)

- 1. Index
- 2. Labeling (check one)  Draft Labeling  Final Printed Labeling
- 3. Summary (21 CFR 314.50(c))
- 4. Chemistry section
  - A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50(d) (1), 21 CFR 601.2)
  - B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
  - C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
- 5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
- 6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
- 7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
- 8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)
- 9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
- 10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
- 11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
- 12. Case report forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
- 13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
- 14. A patent certification with respect to any patent which claims the drug (21 U.S.C.355 (b) (2) or (j) (2) (A))
- 15. Establishment description (21 CFR Part 600, if applicable)
- 16. Debarment certification (FD&C Act 306 (k) (1))
- 17. Field copy certification (21 CFR 314.50(k) (3))
- 18. User Fee Cover Sheet (Form FDA 3397)
- 19. OTHER (Specify)

**CERTIFICATION**

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT

TYPED NAME AND TITLE

Markus F. Herzig, Executive Director Regulatory Affairs

DATE

May 18, 2000

ADDRESS (Street, City, State, and ZIP Code)

732 Louis Drive  
Warminster, PA 18974

TELEPHONE NUMBER

215-956-2200

Public reporting burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer  
Paperwork Reduction Project (0910-0338)  
Hubert H. Humphrey Building, Room 531-H  
200 Independence Avenue, S.W.  
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please DO NOT RETURN this form to this address.

Correspondence from Applicant

07-21-00

**ORAPHARMA, INC.**

www.orapharma.com

NEW CORRESP  
NC

732 Louis Drive

Warminster, PA 18974

215/956-2200 Tel

215/443-9531 Fax

July 21, 2000

Ms. Kalyani Bhatt – DESK COPY  
Division of Dermatologic / Dental Drug Products  
Center for Drug Evaluation & Research  
Food and Drug Administration  
9201 Corporate Boulevard  
Rockville, MD 20850

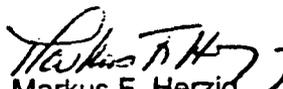
NDA – 50-781  
ARESTIN (Minocycline HCl)  
DESK COPY of Floppy Disk

Dear Ms. Bhatt:

Enclosed are two floppy disks containing the Phase 3 protocol for studies OPI-103A and B and the latest draft package insert which was included in our 120 day safety update.

I provided you with two disks just as a safety measure in case one is defective.

Sincerely,

  
Markus F. Herzig  
Executive Director Regulatory Affairs

MFH:stk

Enclosure



**Correspondence from Applicant**

**06-29-00**