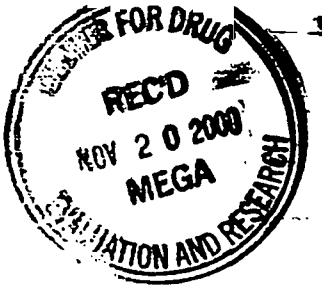
\PHARMA, INC.
/ww.orapharma.com

Warminster, PA 18974
215/956-2200 Tel
215/443-9531 Fax



November 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

NEW
NC

RE: NDA 50-781
Minocycline PTS-
Amendment: Requested Financial Interest Information

Dear Dr. Wilkin:

Enclosed is the corrected form FDA 3454 as requested by Ms. Bhatt.

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

S ely,

Markus F. Herzig

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

Form FDA 356h
Submitted in duplicate

ORIGINAL

Correspondence from Applicant
11-9-00

ORAPHARMA, INC.
www.orapharma.com

732 Louis Drive
Warminster, PA 18974
215/956-2200 Tel
215/443-9531 Fax

NDA ORIG AMENDMENT

November 9, 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

BC

RE: NDA 50-781
Minocycline PTS
Amendment: CMC - Unit Dose Dispenser Identifier

Dear Dr. Wilkin:

Reference is made to a telephone conversation between Drs. DeCamp, Gautam-Basak, and Ms. Bhatt in your Division and Dr. Lawter and Mr. Herzig of OraPharma, Inc. in which Dr. DeCamp inquired how OraPharma intends to place an identifier on each unit dose dispenser.

Dr. Lawter stated that we intend to add the identifier "OP-1" on each molded unit dose dispenser. This was found acceptable by the FDA representatives and Dr. DeCamp asked to have the revised dispenser drawings submitted as an amendment including a suggested text change in the "How Supplied" section of the draft package insert.

Enclosed are drawings of the old dispenser and the new commercial dispenser tip showing the raised identifier "OP-1" in the molded unit dose dispensers. Also enclosed is the revised "How Supplied" section of the draft package insert stating the addition of the identifier on each unit dose dispenser.

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

ORIGINAL

Form FDA 356h
Submitted in duplicate

Correspondence from Applicant
11-6-00

APHARMA, INC.
www.orapharma.com

732 Louis Drive
Warminster, PA 18974
215/956-2200 Tel
215/443-9531 Fax

November 6, 2000

NDA ORIG AMENDMENT

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

DC

RE: NDA 50-781
Minocycline PTS
Amendment: CMC-Stability Update

Dear Dr. Wilkin:

OraPharma, Inc. is amending the pending NDA 50-781 with the attached stability update.

If you have any questions regarding this submission, please call 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
11-3-00

ORAPHARMA, INC.
www.orapharma.com

732 Louis Drive
Warminster, PA 18974
215 956-2200 Tel
215 443-9531 Fax

November 3, 2000

NDA ORIG AMENDMENT

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

BC

RE: NDA 50-781
Minocycline PTS
Amendment: CMC Information Amendment

Dear Dr. Wilkin:

During the FDA PAI inspection at Packaging Coordinators, Inc. (PCI), the company where our product "ARESTIN" will be filled and packaged, the inspector recommended we amend our NDA to include more detailed information on our filling machine.

The ———— filling machine described in this NDA amendment is the filling machine first described in the IND —— Serial #046 submitted on June 29, 1998. This filling machine was used to produce the Phase 3 clinical dispensers as well as the NDA stability batches dispensers.

Detailed descriptions and pictures have not been provided previously and are included in this submission for comparison purposes, along with the filling machine which we plan to use commercially the————.

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

DUPLICATE

Form FDA 356h
Submitted in duplicate

Correspondence from Applicant
11-3-00

RAPHARMA, INC.
www.orapharma.com

732 Louis Drive
Warminster, PA 18974

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

November 3, 2000

NDA ORIG AMENDMENT

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

BM

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

Dear Dr. Wilkin:

Reference is made to a teleconference held on November 2, 2000 between Drs. Gilkes, Hyman and Ms. Bhatt from your division and Dr. Lessem and Mr. Herzig from OraPharma, Inc. The medical review team requested additional information. Dr. Hyman identified that a narrative of an SAE patient was missing from the 120 day safety update submitted on June 16, 2000 as amendment 4.1. Further, Dr. Hyman stated that he would like a summary of all the discontinued patients from our studies OPI-103A, OPI-103B, and OPI-104. He informed OraPharma that the statistician stated that the numbers do not add up correctly.

Dr. Hyman asked when we would be able to submit this information and added that he would appreciate it if we could provide it before November 6, 2000 PM as the FDA has a meeting scheduled to discuss this NDA. Dr. Lessem told Dr. Human that we would supply his requested information before the FDA's meeting time.

Attached herewith is the additional narrative for patient 01-027, and copies of all the discontinuation sections from the referenced studies (OPI-103A, OPI-103B, OPI-104 as well as the ISS and ISE).

I hope the information provided clarifies the medical review teams questions, but please don't hesitate to call me if additional information needed.

Sincerely,

Markus F. Herzig

ORIGINAL

Executive Director, Regulatory Affairs and Quality Assurance

Form FDA 356h
Submitted in duplicate

Correspondence from Applicant
10-9-00

ORAPHARMA, INC.
www.orapharma.com

732 Louis Drive
Warminster, PA 18974
215/956-2200 Tel
215/443-9531 Fax

October 9, 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
Minocycline PTS
Amendment: Tradename Commitment

Dear Dr. Wilkin:

Our response to the recently received telefax (October 6, 2000, attached) from your Division regarding the acceptability of the tradename "ARESTIN" for our product we commit the two points raised in the telefax.

OraPharma will undertake the effort to have all reference sources that contain the discontinued Arestin (trimethobenzamide) removed from the referenced material. We will undertake a thorough search and inform the publishers/editors of these reference books.

OraPharma also agrees to change the name of our product if post-marketing reports reveal that the wrong drug (trimethobenzamide) was administered.

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT OraPharma, Inc.	DATE OF SUBMISSION October 9, 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 ARESTIN™
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

PLICATION 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

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

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 review 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	DATE
Markus F. Herzig	Markus F. Herzig, Executive Director Regulatory Affairs	October 9, 2000

ADDRESS *(Street, City, State, and ZIP Code)*	TELEPHONE NUMBER
732 Louis Drive Warminster, PA 18974	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.

This is in response to a May 8, 2000 meeting request from Orapharma, Inc for a meeting to discuss their proposed proprietary name of Arestin PTS.

The tradename will be acceptable on the following conditions.

1.) The firm has agreed to undertake a comprehensive effort to update any and all reference sources that contain a mention of the discontinued ARESTIN (trimethobenzamide) product. We would ask for a written commitment to that effect and that the firm provide the Agency with documentation of their search and the actions taken to remedy any reference book notations.

2.) We ~~would~~ also request that a post-marketing commitment be made to (1) treat all expedited reports and (2) be willing to change the name of the product if post-marketing reports are received that led to a patient receiving the wrong drug (trimethobenzamide).