

**CENTER FOR DRUG  
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RESEARCH**

**APPLICATION NUMBER:**

**65-156**

**CHEMISTRY REVIEW(S)**



# **ANDA 65-156**

**Minocycline Hydrochloride Tablets USP, 50 mg, 75 mg, and 100 mg**

**Ranbaxy Laboratories Limited**

**M. Scott Furness**

**Division of Chemistry II, Office of Generic Drugs**



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**APPEARS THIS WAY  
ON ORIGINAL**



# Chemistry Review Data Sheet

1. ANDA: **65-156**
2. REVIEW #1
3. REVIEW DATE: 30-MAY-2003
4. REVIEWER: M. Scott Furness
5. PREVIOUS DOCUMENTS:

<b>Previous Documents</b>	<b>Document Date</b>
Original Submission	10-FEB-2003
Telephone Amendment	19-MAR-2003
Telephone Amendment	20-MAR-2003
Telephone Amendment	25-MAR-2003
Acceptable for Filing Notice	31-MAR-2003

6. SUBMISSION(S) BEING REVIEWED:

<b>Submission(s) Reviewed</b>	<b>Document Date</b>
Original Submission	10-FEB-2003
Amendment	19-MAR-2003
Amendment	20-MAR-2003
Amendment	25-MAR-2003

7. NAME & ADDRESS OF APPLICANT:

<b>Name:</b>	Ranbaxy Laboratories Limited
<b>Address:</b>	Sector 18, Udyog Vihar Industrial Area Gurgaon – 122 001, India
<b>U.S. Agent:</b>	Ranbaxy Pharmaceuticals Inc. 600 College Road East Princeton, NJ 08540
<b>Representative:</b>	Abha Pant
<b>Telephone:</b>	Phone: (609)-720-5666 Fax: (609)-514-9797



## Chemistry Review Data Sheet

## 8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: N/A  
b) Non-Proprietary Name: Minocycline Hydrochloride Tablets USP, 50 mg, 75 mg, and 100 mg

## 9. LEGAL BASIS FOR SUBMISSION

Reference Listed drug product for the 50 mg and 100 mg strengths: Minocin<sup>®</sup> Tablets, manufactured by Lederle, approved in NDA #50-451. It should be noted that Lederle withdrew Minocin<sup>®</sup> Tablets (50 mg and 100 mg strength) for sale and distribution in 1996. The Agency has reviewed its records and determined that this drug product was not withdrawn from sale for reasons of safety or efficacy (see Federal Register, Vol. 63, 1/27/98 found on pp. 11-12 of the original submission). This allows the Agency to approve ANDAs for Minocycline Hydrochloride tablets which then is the basis for this ANDA submission. A copy of the Suitability Petition approval letter (#98 P-0213/CP1) authorizing the 75 mg tablet was provided in the firm's 3/20/2003 telephone amendment. Signed patent certification and exclusivity statements were provided on p. 16 of the original submission. According to the Orange Book, the reference listed drug is not covered by a listed patent. The proposed drug product contains the same active ingredient and has the same dosage form, route of administration, indication, and usage as the reference listed drug.

## 10. PHARMACOL. CATEGORY: Antibacterial

## 11. DOSAGE FORM: Tablets

## 12. STRENGTH/POTENCY: 50 mg, 75 mg, and 100 mg

## 13. ROUTE OF ADMINISTRATION: Oral

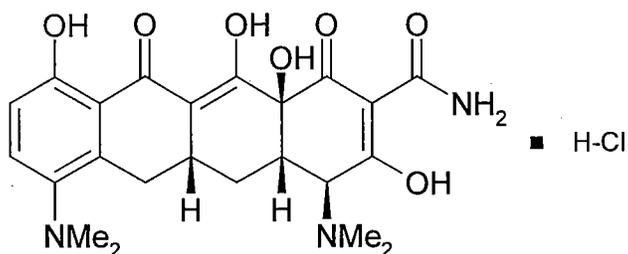
14. Rx/OTC DISPENSED:  Rx  OTC15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

Not a SPOTS product

## 16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

## Chemistry Review Data Sheet



Name: 4,7-Bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-2-naphthacencarboxamide monohydrochloride

Molecular Formula:  $C_{23}H_{27}N_3O_7 \cdot HCl$

Molecular Weight: 493.95

### 17. RELATED/SUPPORTING DOCUMENTS:

#### A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCE	CODE <sup>1</sup>	STATUS <sup>2</sup>	DATE REVIEW COMPLETED	COMMENTS
	II			1	Adequate	4/3/2003	-
	IV			3,4	Adequate	5/7/2003	-
	III			3,4	Adequate	4/29/2002	-
	III			3,4	Adequate	4/29/2002	-
	III			3,4	Adequate	4/29/2002	-
	III			4	-	-	-
	III			3,4	Adequate	7/17/2002	-
	III			4	-	-	-
	III			4	-	-	-
	III			4	-	-	-
	III			4	-	-	-
	III			3,4	Adequate	8/3/2001	-
	III			4	-	-	-
	III			3,4	Adequate	4/14/2003	-

<sup>1</sup> Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted



# CHEMISTRY REVIEW



## Chemistry Review Data Sheet

6 – DMF not available  
7 – Other (explain under "Comments")

<sup>2</sup> Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

**B. Other Documents:** N/A

### 18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES	Satisfactory	4/2/03	J. D. Ambrogio
Labeling	Pending	-	-
Bioequivalence	Pending	-	-

### 19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.  Yes  No If no, explain reason(s) below:

**APPEARS THIS WAY  
ON ORIGINAL**



# The Chemistry Review for ANDA 65-156

## The Executive Summary

### I. Recommendations

- A. **Recommendation and Conclusion on Approvability**  
Not-Approvable (MINOR)
- B. **Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable**  
N/A

### II. Summary of Chemistry Assessments

- A. **Description of the Drug Product(s) and Drug Substance(s)**  
The reference listed drug for this application is Minocin<sup>®</sup> Tablets, manufactured by Lederle, approved in NDA #50-451.

The drug substance is Minocycline Hydrochloride USP and it has a 3-year expiration date.

The drug product is Minocycline Hydrochloride Tablets USP, 50 mg, 75 mg, and 100 mg. The tablets are being marketed in HDPE Bottles with counts of 6's and 500's of each strength. The formulation did not include the use of any novel inactive ingredients.





Executive Summary Section

In-process controls included tablet weight, hardness, friability, and disintegration measurements.

Ranbaxy is proposing a 24-month expiration dating period for the drug product. The proposed expiration date is supported by 3 months of accelerated and long-term stability data.

**B. Description of How the Drug Product is Intended to be Used**

N/A

**C. Basis for Approvability or Not-Approval Recommendation**

Not-Approvable (MINOR)

**III. Administrative**

cc: ANDA 65-156  
ANANDA DUP  
DIV FILE  
Field Copy

Endorsements (Draft and Final with Dates):

HFD-643/SFurness/5/30/03

HFD-643/RAdams/6/18/03

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F/T by: EW 6/20/03

**TYPE OF LETTER:** Not-Approvable (MINOR)

**Redacted**

14

**Page(s) of trade**

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**confidential**

**commercial**

**information**



## **ANDA 65-156**

**Minocycline Hydrochloride Tablets USP, 50 mg, 75 mg, and 100 mg**

**Ranbaxy Laboratories Limited**

**M. Scott Furness  
Division of Chemistry II, Office of Generic Drugs**



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**APPEARS THIS WAY  
ON ORIGINAL**



# Chemistry Review Data Sheet

1. ANDA: 65-156
2. REVIEW #2
3. REVIEW DATE: 30-JUL-2003
4. REVIEWER: M. Scott Furness
5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
Original Submission	10-FEB-2003
Telephone Amendment	19-MAR-2003
Telephone Amendment	20-MAR-2003
Telephone Amendment	25-MAR-2003
Acceptable for Filing Notice	31-MAR-2003
CMC Minor Amendment	26-JUN-2003
Telephone Amendment	25-JUL-2003
Telephone Amendment	28-JUL-2003

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
CMC Minor Amendment	26-JUN-2003
Telephone Amendment	25-JUL-2003
Telephone Amendment	28-JUL-2003

7. NAME & ADDRESS OF APPLICANT:

<b>Name:</b>	Ranbaxy Laboratories Limited
<b>Address:</b>	Sector 18, Udyog Vihar Industrial Area Gurgaon – 122 001, India Ranbaxy Pharmaceuticals Inc.
<b>U.S. Agent:</b>	600 College Road East Princeton, NJ 08540
<b>Representative:</b>	Abha Pant
<b>Telephone:</b>	Phone: (609)-720-5666 Fax: (609)-514-9797



## Chemistry Review Data Sheet

## 8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A

b) Non-Proprietary Name: Minocycline Hydrochloride Tablets USP, 50 mg, 75 mg, and 100 mg

## 9. LEGAL BASIS FOR SUBMISSION

At the time of submission the Reference Listed drug product for the 50 mg and 100 mg strengths was Minocin<sup>®</sup> Tablets, manufactured by Lederle, approved in NDA #50-451. It should be noted that Lederle withdrew Minocin<sup>®</sup> Tablets (50 mg and 100 mg strength) for sale and distribution in 1996. The Agency reviewed its records and determined that this drug product was not withdrawn from sale for reasons of safety or efficacy (see Federal Register, Vol. 63, 1/27/98 found on pp. 11-12 of the original submission). This allows the Agency to approve ANDAs for Minocycline Hydrochloride tablets which then is the basis for this ANDA submission. A copy of the Suitability Petition approval letter (#98 P-0213/CP1) authorizing the 75 mg tablet was provided in the firm's 3/20/2003 telephone amendment. Signed patent certification and exclusivity statements were provided on p. 16 of the original submission. According to the Orange Book, the reference listed drug is not covered by a listed patent. The proposed drug product contains the same active ingredient and has the same dosage form, route of administration, indication, and usage as the reference listed drug.

With the approval of Medicis ANDA 65-131 for Minocycline Tablets USP, 50 mg, 75 mg, and 100 mg, this has become the RLD. Ranbaxy submitted amended Form 356h, amended Basis of Submission, and revised patent and exclusivity certification to reflect this.

10. PHARMACOL. CATEGORY: Antibacterial

11. DOSAGE FORM: Tablets

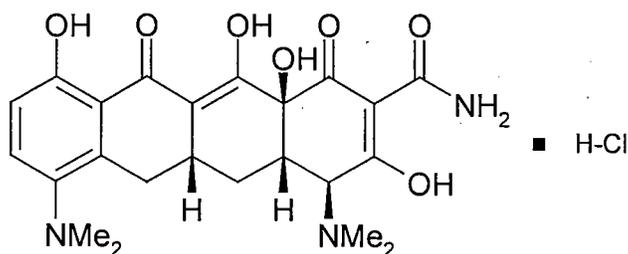
12. STRENGTH/POTENCY: 50 mg, 75 mg, and 100 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED:  Rx  OTC15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM): SPOTS product – Form Completed Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

## Chemistry Review Data Sheet



Name: 4,7-Bis(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-2-naphthacencarboxamide monohydrochloride

Molecular Formula:  $C_{23}H_{27}N_3O_7 \cdot HCl$

Molecular Weight: 493.95

**17. RELATED/SUPPORTING DOCUMENTS:**
**A. DMFs:**

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE <sup>1</sup>	STATUS <sup>2</sup>	DATE REVIEW COMPLETED	COMMENTS
	II			1	Adequate	4/3/2003	-
	IV			3,4	Adequate	5/7/2003	-
	III			3,4	Adequate	4/29/2002	-
	III			3,4	Adequate	4/29/2002	-
	III			3,4	Adequate	4/29/2002	-
	III			4	-	-	-
	III			3,4	Adequate	7/17/2002	-
	III			4	-	-	-
	III			4	-	-	-
	III			4	-	-	-
	III			4	-	-	-
	III			3,4	Adequate	8/3/2001	-
	III			4	-	-	-
	III			3,4	Adequate	4/14/2003	-

<sup>1</sup> Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted



# CHEMISTRY REVIEW



## Chemistry Review Data Sheet

6 – DMF not available

7 – Other (explain under "Comments")

<sup>2</sup> Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

**B. Other Documents:** N/A

### 18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES	Satisfactory	4/2/03	J. D. Ambrogio
Labeling	Satisfactory	11/6/03	A.Vezza
Bioequivalence	Satisfactory	12/12/03	L.Chuang

### 19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.  Yes  No If no, explain reason(s) below:

**APPEARS THIS WAY  
ON ORIGINAL**

# The Chemistry Review for ANDA 65-156

## The Executive Summary

### I. Recommendations

- A. **Recommendation and Conclusion on Approvability**  
Approval is recommended.
- B. **Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable**  
N/A

### II. Summary of Chemistry Assessments

- A. **Description of the Drug Product(s) and Drug Substance(s)**  
The reference listed drug for this application is Minocin<sup>®</sup> Tablets, manufactured by Lederle, approved in NDA #50-451.

The drug substance is Minocycline Hydrochloride USP and it has a 3-year expiration date.

The drug product is Minocycline Hydrochloride Tablets USP, 50 mg, 75 mg, and 100 mg. The tablets are being marketed in HDPE Bottles with counts of 6's and 500's of each strength. The formulation did not include the use of any novel inactive ingredients.





Executive Summary Section

In-process controls included tablet weight, hardness, friability, and disintegration measurements.

Ranbaxy is proposing a 24-month expiration dating period for the drug product. The proposed expiration date is supported by 3 months of accelerated stability data and 9 months of long-term stability data.

- B. Description of How the Drug Product is Intended to be Used**  
N/A
- C. Basis for Approvability or Not-Approval Recommendation**  
Approval is recommended.

**III. Administrative**

cc: ANDA 65-156  
DIV FILE  
Field Copy

Endorsements (Draft and Final with Dates):

HFD-643/SFurness/7/30/03; 12/17/03 (upon completion of bio review) *M. Seth Furness 12/18/03*

HFD-643/RAdams/8/1/03; 12/17/03 *R-C Adams 12/18/03*

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F/T by:mda/12/17/03

**TYPE OF LETTER:** Approval

**Redacted** 16.

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**commercial**

**information**