CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65115

CHEMISTRY REVIEW(S)

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Abbreviated New Drug Application Review

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1. CHEMISTRY REVIEW NO. 1

2. ANDA # 65-115

3. NAME AND ADDRESS OF APPLICANT
Ranbaxy Laboratories Limited
Sector 18, Udyog Vihar Industrial Area
Gurgaon - 122 001, India

U.S. Agent:
Abha Pant, US Agent
Ranbaxy Pharmaceuticals Inc
600 College Road East
Princeton, NJ 08540

Phone: (609) 720-5666
Fax: (609) 720-1155

4. LEGAL BASIS FOR SUBMISSION
The application is based on Duricef® for Oral Suspension manufactured by Bristol Myers Squibb (NDA# 50-527). The firm states that no effective patents or exclusivity periods are in force for the referenced product.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Cefadroxil for Oral Suspension, USP

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:
Firm:
Original Submission: 12/17/01
Bioequivalence Amendment: 3/13/02

FDA:
Acceptance for filing: 2/6/02

10. PHARMACOLOGICAL CATEGORY
Antibacterial

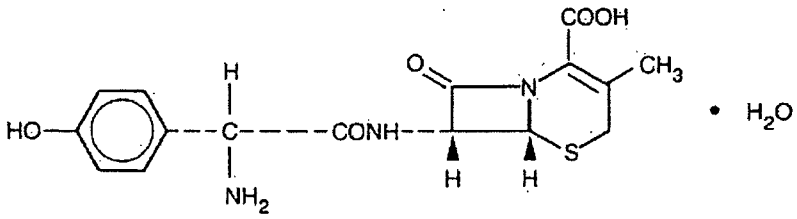
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Powder for oral suspension

14. POTENCIES
125 mg/5 mL, 250 mg/5 mL, and 500 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
$C_{16}H_{17}N_3O_5S \cdot H_2O$ 381.40



5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[amino(4-hydroxy-phenyl)acetyl] amino]-3-methyl-8-oxo-, monohydrate, [6R-[6(alpha),7(beta)(R*)]]-.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
The application is not approvable for minor chemistry deficiencies.

18. CONCLUSIONS AND RECOMMENDATIONS
Not Approvable (Minor)

19. REVIEWER: Ruth Ganunis
DATE COMPLETED: 3/25/02

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Chem Review #1

APR 11 20[redacted]

Chemistry Comments to be Provided to the Applicant

ANDA: 65-115 APPLICANT: Ranbaxy Laboratories Limited

DRUG PRODUCT: Cefadroxil for Oral Suspension USP,
125 mg/5 mL, 250 mg/5 mL, and 500 mg/5 mL

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. The drug substance specification limits for total degradation products and total impurities are not justified by the levels found in the data provided.

2. The drug substance specification limits for residual solvents are not justified by the levels found in the data provided.

3. Please clarify what is meant by

4. The in-process specification sheet for the 500 mg/5 mL strength does not include a test and specification for Uniformity of Weight. The specification is included on the report forms for the exhibit batches. Please clarify.

5. The finished product and stability specification limits for total related substances are not justified by the levels found in the data provided.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The Drug Master File (DMF) for Cefadroxil Monohydrate was reviewed and found deficient. The DMF holder has been informed of the deficiencies.

2. If available, please provide updated stability data in your next amendment.

Sincerely yours,

/S/

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Abbreviated New Drug Application Review

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1. CHEMISTRY REVIEW NO. 2

2. ANDA # 65-115

3. NAME AND ADDRESS OF APPLICANT
Ranbaxy Laboratories Limited
Sector 18, Udyog Vihar Industrial Area
Gurgaon - 122 001, India

U.S. Agent:
Abha Pant, US Agent
Ranbaxy Pharmaceuticals Inc
600 College Road East
Princeton, NJ 08540

Phone: (609) 720-5666
Fax: (609) 720-1155

4. LEGAL BASIS FOR SUBMISSION
The application is based on Duricef® for Oral Suspension manufactured by Bristol Myers Squibb (NDA# 50-527). The firm states that no effective patents or exclusivity periods are in force for the referenced product.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Cefadroxil for Oral Suspension, USP

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:
Firm:
Original Submission: 12/17/01
Bioequivalence Amendment: 3/13/02
Bioequivalence Amendment: 6/14/02
Chemistry Amendment: 6/14/02

FDA:
Acceptance for filing: 2/6/02
Chemistry review 1, not acceptable: 3/25/02
Bioequivalence review acceptable: 5/22/02

10. PHARMACOLOGICAL CATEGORY
Antibacterial

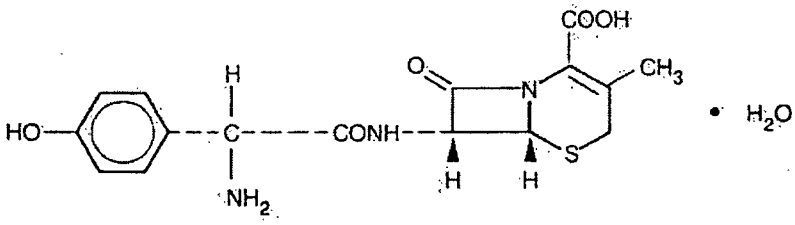
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Powder for oral suspension

14. POTENCIES
125 mg/5 mL, 250 mg/5 mL, and 500 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
$C_{16}H_{17}N_3O_5S \bullet H_2O$ 381.40



5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[amino(4-hydroxy-phenyl)acetyl] amino]-3-methyl-8-oxo-, monohydrate, [6R-[6(alpha),7(beta)(R*)]]-.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
Labeling, pending
Bioequivalence, pending
EER, pending

The subject of this review is the 6/14/02 chemistry amendment.

18. CONCLUSIONS AND RECOMMENDATIONS
Not Approvable (Minor)

19. REVIEWER: DATE COMPLETED:
Ruth Ganunis 7/25/02

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Chem. Review #2

AUG 13 2002

Chemistry Comments to be Provided to the Applicant

ANDA: 65-115 APPLICANT: Ranbaxy Laboratories Limited

DRUG PRODUCT: Cefadroxil for Oral Suspension USP,
125 mg/5 mL, 250 mg/5 mL, and 500 mg/5 mL

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Please provide updated finished product and stability test methods that include the Dissolution test.

2. Please provide methods validation data for method for Dissolution.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

DMF was reviewed and found not adequate. The DMF holder has been informed of the deficiencies.

Sincerely yours,

/S/

for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Abbreviated New Drug Application Review

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1. CHEMISTRY REVIEW NO. 3

2. ANDA # 65-115

3. NAME AND ADDRESS OF APPLICANT
Ranbaxy Laboratories Limited
Sector 18, Udyog Vihar Industrial Area
Gurgaon - 122 001, India

U.S. Agent:
Abha Pant, US Agent
Ranbaxy Pharmaceuticals Inc
600 College Road East
Princeton, NJ 08540

Phone: (609) 720-5666
Fax: (609) 720-1155

4. LEGAL BASIS FOR SUBMISSION
The application is based on Duricef® for Oral Suspension manufactured by Bristol Myers Squibb (NDA# 50-527). The firm states that no effective patents or exclusivity periods are in force for the referenced product.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Cefadroxil for Oral Suspension, USP

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:
Firm:
Original Submission: 12/17/01
Bioequivalence Amendment: 3/13/02
Bioequivalence Amendment: 6/14/02
Chemistry Amendment: 6/14/02
Chemistry Amendment: 10/11/02

FDA:
Acceptance for filing: 2/6/02
Chemistry review 1, not acceptable: 3/25/02
Bioequivalence review acceptable: 5/22/02
Addendum to Bioequivalence review acceptable: 12/20/02
Chemistry review 2, not acceptable: 8/13/02

10. PHARMACOLOGICAL CATEGORY
Antibacterial

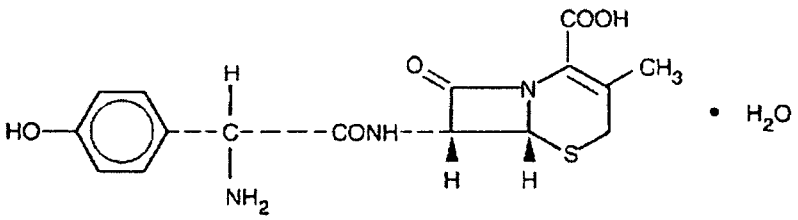
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Powder for oral suspension

14. POTENCIES
125 mg/5 mL, 250 mg/5 mL, and 500 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
$C_{16}H_{17}N_3O_5S \cdot H_2O$ 381.40



5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[amino(4-hydroxy-phenyl)acetyl] amino]-3-methyl-8-oxo-, monohydrate, [6R-[6(alpha),7(beta)(R*)]]-.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
Labeling, pending
Bioequivalence: acceptable
EER, pending

The subject of this review is the 10/11/02 chemistry amendment.

18. CONCLUSIONS AND RECOMMENDATIONS
Not Approvable (Telephone)

19. REVIEWER: Yanping Pan
DATE COMPLETED: 1/3/02

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Chem. Review #3

Chemistry Comments to be Provided to the Applicant

ANDA: 65-115 APPLICANT: Ranbaxy Laboratories Limited

DRUG PRODUCT: Cefadroxil for Oral Suspension USP,
125 mg/5 mL, 250 mg/5 mL, and 500 mg/5 mL

The deficiencies presented below represent **Telephone** deficiencies.

A. Deficiency:

The dissolution test method provided in Attachment 1, Minor Amendment dated 10/11/02 is not updated (method with Paddle speed rpm, rather than rpm as you accepted per Bioequivalence comments acknowledgement dated December 6, 2002). Please revise and provide updated finished product and stability test methods which include updated Dissolution test.

Sincerely yours,

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Abbreviated New Drug Application Review

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1. CHEMISTRY REVIEW NO. 3a

2. ANDA # 65-115

3. NAME AND ADDRESS OF APPLICANT
Ranbaxy Laboratories Limited
Sector 18, Udyog Vihar Industrial Area
Gurgaon - 122 001, India

U.S. Agent:
Abha Pant, US Agent
Ranbaxy Pharmaceuticals Inc
600 College Road East
Princeton, NJ 08540

Phone: (609) 720-5666
Fax: (609) 720-1155

4. LEGAL BASIS FOR SUBMISSION
The application is based on Duricef® for Oral Suspension manufactured by Bristol Myers Squibb (NDA# 50-527). The firm states that no effective patents or exclusivity periods are in force for the referenced product.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Cefadroxil for Oral Suspension, USP

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:
Firm:
Original Submission: 12/17/01
Bioequivalence Amendment: 3/13/02
Bioequivalence Amendment: 6/14/02
Chemistry Amendment: 6/14/02
Chemistry Amendment: 10/11/02
Chemistry Telephone Amendment:1/22/03

FDA:
Acceptance for filing: 2/6/02
Chemistry review 1, not acceptable: 3/25/02
Bioequivalence review acceptable: 5/22/02
Addendum to Bioequivalence review acceptable: 12/20/02
Chemistry review 2, not acceptable: 8/13/02
Chemistry review 3, not Acceptable (Telephone): 1/3/03

10. PHARMACOLOGICAL CATEGORY
Antibacterial

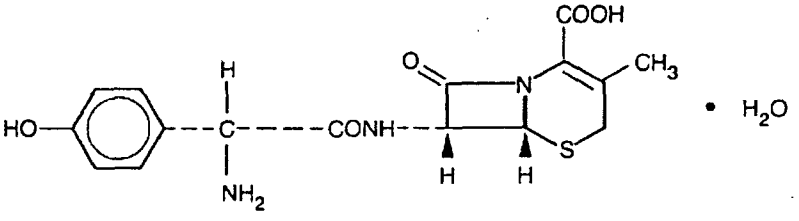
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Powder for oral suspension

14. POTENCIES
125 mg/5 mL, 250 mg/5 mL, and 500 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
$C_{16}H_{17}N_3O_5S \cdot H_2O$ 381.40



5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[amino(4-hydroxy-phenyl)acetyl] amino]-3-methyl-8-oxo-, monohydrate, [6R-[6(alpha),7(beta)(R*)]]-.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
Labeling: acceptable
Bioequivalence: acceptable
EER: Acceptable as 2/10/03
DMF# Adequate as 3/25/03 (Reviewed by Y. Pan)

The subject of this review is the 1/22/03 chemistry Telephone Amendment.

18. CONCLUSIONS AND RECOMMENDATIONS
Approvable (Pending EER acceptable)

19. REVIEWER: Yanping Pan
DATE COMPLETED: 2/5/03, revised 3/25/03

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Chem. Review # 3a