

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

65-056

CHEMISTRY REVIEW(S)

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

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 65-056

3. NAME AND ADDRESS OF APPLICANT

TEVA Pharmaceuticals
1510 Delp Drive
Kulpsville, PA 19443

Phone: (215) 256-8400

Fax: (215) 256-8105

U.S. Agent

N/A

4. LEGAL BASIS FOR SUBMISSION

The application is based on Amoxil® Tablets manufactured by Smithkline Beecham (NDA# 50-754). The firm states that no effective patents or exclusivity periods are in force for the referenced product (pp. 11, 16).

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Amoxicillin Tablets, USP

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

Firm:

Original Submission: 12/3/99

Amendment, colorant formulation: 12/21/99

Amendment, Bio: 2/14/00

Amendment, Bio: 2/29/00

Amendment, Chemistry and Labeling: 6/30/00

Amendment, Chemistry: 8/30/00

FDA:

Acceptance for filing: 1/27/00
 Labeling, deficient: 3/3/00
 Bioequivalence, acceptable: 3/7/00
 Chemistry and Labeling, deficient: 6/5/00
 Labeling Deficient: 7/17/00
 Chemistry Telephone Amendment: 8/28/00, 8/29/00

10. PHARMACOLOGICAL CATEGORY

Antibacterial

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM

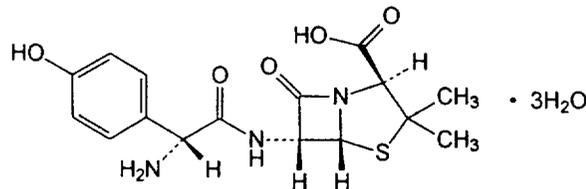
Tablet

14. POTENCIES

500 and 875 mg

15. CHEMICAL NAME AND STRUCTURE

Amoxicillin. 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[amino-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo, trihydrate [2S-[2 α ,5 α ,6 β (S*)]]-.
 $C_{16}H_{19}N_3O_5S \cdot 3H_2O$. 419.46. 61336-70-7. Antibacterial.



16. RECORDS AND REPORTS

N/A

17. COMMENTS

Upon review, Dr. Vilayat Sayeed made the comments highlighted below. These concerns were communicated to the firm by telephone on August 28 and 29, 2000. The firm's August 30, 2000 telephone amendment response are provided below.

Comment: The stability data does not support the proposed water specification of The firm was requested to reduce the specification for water on stability to as for finished product release.

Response: The firm reduced the specification for water on stability to The firm provided the revised Finished Product Procedures Manual and Finished Product Stability Protocol which reflect the change.

Comment: TEVA has two sets of impurity specifications for the drug substance on pages 1841 and 1842. The firm was asked to clarify.

Response: The firm responded, "While the impurity specifications listed on page 1841 of our original application contained the drug substance manufacturer's stability limits of Largest Individual and Total we do not intend to accept material which does not comply with Teva USA's limits of Largest Individual and Total as listed in our laboratory procedure manual for the bulk drug."

First Generic
 DMF, acceptable: 5/22/00
 Labeling, acceptable: 8/18/00
 Bioequivalence, acceptable: 3/7/00
 EER, acceptable: 7/17/00

18. CONCLUSIONS AND RECOMMENDATIONS

Recommend approval

19. REVIEWER:

Ruth Ganunis

DATE COMPLETED:

7/24/00

Page(s) 14

Contain Trade Secret,
Commercial/Confidential
Information and are not
releasable.

Chem Rev. 2

7/24/00

JUN 5 2000

38. Chemistry Comments to be Provided to the Applicant

ANDA: 65-056

APPLICANT: Teva Pharmaceuticals USA

DRUG PRODUCT: Amoxicillin Tablets USP, 500 mg and 850 mg

The deficiencies presented below represent FAX deficiencies.

A. Deficiencies:

1. Please describe the maximum holding time for the bulk finished product in the lined fiber drums prior to packaging in the market containers. Please note that up to a 30 day holding time is permitted without supporting data.
2. We note that the proposed PF monograph for Amoxicillin Tablets, USP eliminates the water specification of . Please include a specification for water in your finished and stability product testing procedures that is supported by your exhibit batch data.

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

1. Since you are obtaining drug substance from TEVA Mexico, MO, you have proposed accepting material based on the COA and an identification test. This is acceptable provided that you have established the reliability of the supplier's analysis through appropriate validation. Please provide confirmation.
2. We note that you are using an alternative method for identification of the drug product. Please be advised that approval to use an alternate method that differs from that in the USP does not release you from any obligations to comply with the methods and procedures in the USP. Therefore, in the event of dispute only the results obtained by the official methods and procedures in the USP will be considered conclusive.

3. If available, please provide updated room temperature stability data in your next amendment.

Sincerely yours,



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