Amoxapine
25 mg, 50 mg, 100 mg and 150 mg tablet
ANDA# 72-418
72-419
72-420
72-421
Reviewer: M. Chen
Wang [redacted]

DEC 20 1988

Watson Laboratories, Inc.
Libertyville, Il.
Submission Date:
Sept. 13, 1988
Sept. 14, 1988
Oct. 10, 1988
November 30, 1988

Review of Dissolution Data and Request of Waiver

The firm has previously conducted an acceptable bioequivalence study on its Amoxapine tablet, 100 mg, as compared to the reference product, Asendin® tablet, 100 mg, manufactured by Lederle Laboratories (submission dated Aug. 2, 1988). In response to the comments made by the agency, the firm has provided the content uniformity data for the lots used in the bioequivalence study. In addition, the firm has resubmitted the dissolution data for the four strengths of Amoxapine tablets using the following conditions:

USP XXI apparatus II at 50 rpm
900 ml simulated gastric fluid (w/o enzyme)
Number of tablets: 12
Sampling time: 10, 20 and 30 minutes

The content uniformity data and results of the dissolution testing are appended to this review.

The firm has indicated the rationale for conducting the bioequivalence study on its Amoxapine 100 mg tablet instead of 150 mg tablet. The firm contends that literature and their communications with clinicians have shown that the most observed side effects of the drug under investigation are drowsiness (a high 14% incidence) and other behavior abnormalities, such as agitation and disorientation. These adverse reactions could be a practical problem during the clinical study, based on their observation in a similar biostudy for Loxapine 50 mg. It was thus recommended by Dr. Korchinski, the medical supervisor of the clinical study, that 150 mg tablet be avoided. The firm further states that this strength (150 mg) is not a commonly prescribed dose.

Comment:

The firm's response for the agency's inquiry regarding the rationale for conducting the bioequivalence study on its Amoxapine 100 mg tablet (instead of 150 mg) is adequate.

Recommendations:

1. The dissolution testing conducted by Watson Laboratories on its Amoxapine tablet, 25 mg, 50 mg, 100 mg and 150 mg, Lot# R09787, R09887, R09987 and R10087, is acceptable.

2. The dissolution testing should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 900 ml of simulated gastric fluid (w/o enzyme) at 37°C using USP XXI apparatus II at 50 rpm. The test product should meet the following specification:

   Not less than 85% of the labelled amount of the drug in the dosage form is dissolved in 30 minutes

3. The firm has previously conducted an acceptable bioequivalence study on its Amoxapine tablet, 100 mg (submission dated Aug. 2, 1988). The formulations for the 25 mg, 50 mg and 150 mg strength are proportionally similar to the 100 mg strength of the test product which underwent bioequivalency testing. Therefore, the waiver of in vivo bioequivalence study requirements for the 25 mg, 50 mg and 150 mg tablet of the test product is granted. The 25 mg, 50 mg and 150 mg tablet of the test product are deemed bioequivalent to the 25 mg, 50 mg and 150 mg tablet of Asendin®, respectively, manufactured by Lederle Laboratories.

3. From the bioequivalence point of view, the firm has met the requirements of in vivo bioavailability and in vitro dissolution testing for its 25 mg, 50 mg, 100 mg and 150 mg Amoxapine tablets.

4. Therapeutic Equivalence Recommendation

   The Division of Bioequivalence recommends that ALL THE TEST PRODUCTS SHOULD BE CODED AB IN THE THERAPEUTIC EQUIVALENCE LIST.

The firm should be informed of the comment and recommendations.

Mei-Ling Chen

Mei-Ling Chen, Ph.D.
Division of Bioequivalence
Review Branch 2

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MChen/MC/12-01-88/Wang [redacted]

cc: ANDA # 72-418, 72-419, 72-420, 72-421 original, HFD-230, HFD-200 (Hare), HFD-22 (Hooton), HFD-255 (Pelsor, Chen), Drug File