CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-775

MICROBIOLOGY REVIEW

Division of Anti-Infective Drug Products (HFD-520)
Clinical Microbiology Review Notes #1

NDA # 50-775 DATE COMPLETED: 21 JUL 1999

APPLICANT(NDA):

Abbott Laboratories
100 Abbott Park Road
Abbott Park, IL 60064-3500

CHEM/THER. TYPE: macrolide

SUBMISSION REVIEWED: Original NDA
PROVIDING FOR: A new extended release dosage form with addition of *Haemophilus parainfluenzae* to the Indications or Microbiology sections of the package insert

PRODUCT NAMES(S):
Proprietary: Biaxin XL

Non-Proprietary/USAN: clarithromycin

DOSAGE FORMS(S) Extended release filmtab

STRENGTHS: 500 mg

ROUTE(S) OF ADMINISTRATION: Oral

PHARMACOLOGICAL CATEGORY: Antiinfective

DISPENSED: X Rx ___ OTC

INITIAL SUBMISSION:
Received by CDER: 4 MAY 1999
Received by Reviewer: 5 MAY 1999
Review Completed: 21JUL 1999

AMENDMENT(S)
Received by CDER: N/A
Received by Reviewer:
Review Completed:

REMARK(S):

From the microbiological perspective only, this NDA can be viewed as a labeling amendment which leads to the addition of a new species, *Haemophilus parainfluenzae*, to the list of microorganisms associated with the Indications and Usage section of the product package insert. To that end, the applicant has provided a summary of the clinical studies, which are purported to demonstrate the activity of clarithromycin against *Haemophilus parainfluenzae*. In vitro data were provided for unrelated species of microorganisms such as penicillin resistant pneumococci but were not evaluated in conjunction with the newly proposed claim for *Haemophilus parainfluenzae*. Clearly, the proposed addition of *Haemophilus parainfluenzae* to the package insert will be approvable from the microbiological perspective if a clinical claim for the organism is approved for inclusion in the Indications and Usage section of the package insert.

From a broader perspective, this NDA also provides for a new extended release dosage form that has a common package insert with the currently approved dosage form. Within that context, the two dosage forms are expected to be bioequivalent from the pharmacokinetic perspective. If the two dosage forms are indeed bioequivalent and the bioequivalence is further supported by clinical studies, then the Microbiology subsection of the currently approved dosage form is applicable to the sustained release dosage form. By inference, the proposed addition of *Haemophilus parainfluenzae* to the package inserts is appropriate for both dosage forms.

CONCLUSIONS and/or RECOMMENDATIONS:

From the Microbiological perspective, this NDA is approvable. The NDA provides for a new extended release dosage form that has a common package insert with 250 and 500 milligram Biaxin tablets. The Microbiology subsection of the combined package insert will only require a modification to accommodate inclusion of *Haemophilus parainfluenzae*. Within that context, the two dosage forms are expected to be bioequivalent from the pharmacokinetic perspective. If the two dosage forms are indeed bioequivalent and the bioequivalence is further supported by clinical studies, then the Microbiology subsection of the 250 and 500 milligram tablet can be easily modified to incorporate *Haemophilus parainfluenzae* and will be applicable to the sustained release dosage form. The proposed addition of *Haemophilus parainfluenzae* to the package inserts is appropriate for both dosage forms.

/S/ 8/17/99

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