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RESEARCH**

APPLICATION NUMBER:

50-807

**CLINICAL PHARMACOLOGY AND
BIOPHARMACEUTICS REVIEW(S)**

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW

NDA 50-807

Drug:	Epirubicin Hydrochloride for Injection
Formulation:	50 mg and 200 mg lyophilized powder epirubicin/vial
Indication:	Epirubicin Hydrochloride for Injection is indicated as a component of adjuvant therapy in patients with evidence of axillary node tumor involvement following resection of primary breast cancer.
Applicant:	Mayne Pharma Inc.
OCP Division:	Division of Clinical Pharmacology 5
OND Division:	Division of Oncology Drug Products
Submission Dates:	7/15/2005
Primary Reviewer:	Angela Yuxin Men, MD., Ph.D.
Acting Team Leader:	Brian Booth, Ph.D.
Type of Submission:	NDA-Original

Executive Summary

The applicant submitted the original NDA 50-807, seeking approval of 50 mg and 200 mg lyophilized powder for Epirubicin Hydrochloride for Injection, in addition to the FDA-approved ELLENCE Injection (epirubicin hydrochloride injection-aqueous solution) (NDA 50-778) as a component of adjuvant therapy in patients with evidence of axillary node tumor involvement following resection of primary breast cancer.

The active ingredient, epirubicin, is the same for both formulations and it is supplied as 50 mg and 200 mg strengths. The contents of these formulations are listed in Table 1. In the proposed lyophilized powder formulation, the lactose has been added and sodium chloride has been removed. Prior to use, Epirubicin Hydrochloride for Injection must be reconstituted with Sterile Water for Injection, USP, resulting in a solution concentration of 2 mg/mL with a pH of 4.7 to 5.0. The addition of lactose is not expected to have any effects on epirubicin pharmacokinetics. No additional clinical data was submitted in NDA 50-807.

Table 1 Contents of Epirubicin Formulations

Components	Purpose	Mayne's Product	Ellence [®]

The following concerns have been conveyed to the CMC and clinical reviewers: 1) effect of pH change from 3.0 to 4.7-5.0 on Epirubicin solubility; 2) potential for precipitation of injection site due to the change of pH; 3) any new toxicity issues regarding local irritation. Please refer to their reviews for the results.

Recommendation

The change in formulation is acceptable to Office of Clinical Pharmacology and Biopharmaceutics.

Angela Yuxin Men, MD, Ph.D.
Reviewer
DCP 5

Brian Booth, Ph.D.
Acting Team Leader, Oncology
DCP 5

CC: NDA 50-807
HFD-150/Division File
HFD-150/Zimmerman, Cortazar, Chen
HFD-860/Huang Rahman, Booth, Men

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/s/

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3/20/2006 09:18:00 AM
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