NDA 20-768
Submission Date: September 3, 2003
September 30, 2003
Drug Name and Formulation: Zomig (zolmitriptan) 5 mg tablet
Sponsor: Astra Zeneca Pharmaceuticals LP, Wilmington, DE 19803
Reviewer: Andre Jackson
Type of Submission: Response to Request for Information and Review of Studies in Healthy Adolescents and Healthy Adults Between Attacks

Summary of Clinical Pharmacology and Biopharmaceutics Findings

The clinical pharmacology and biopharmaceutics information submitted to NDA 20-768 is acceptable. However discussions with the medical officer indicate that based upon the pediatric study decision tree the firm will have to conduct another efficacy study for Zolmitriptan in adolescents since the current study failed.

The firm has submitted three studies to address issues from a pediatric written request issued by the Agency on March 26, 1999. Issues for the written request were:
1) a safety and tolerability study in adolescents and adults
2) pharmacokinetic study (in adolescents with a history of migraine)
3) one controlled efficacy trial and a long term safety trial in adolescents and adults

The PK studies submitted by the firm to address the PK issues were:

1) zolmitriptan tablets in healthy adolescents and healthy adults between attacks (Trial 311CIL/0092)
2) zolmitriptan tablets in adult migraineurs both during and between attacks (Trial 136-007)
3) zolmitriptan nasal spray in adolescent migraineurs and adult migraineurs between attacks (Trial D1221C000004).

Systemic exposure to zolmitriptan appeared to be slightly higher in adolescents in comparison with adults. However, although mean Cmax, AUC(0-t), and AUC values were approximately 10% greater in the adolescents the 90% confidence intervals for ratios were in the range of 0.89 to 1.43. In adolescents and adults, Cmax values ranged from 3.7 to 20.3 ng/ml and from 3.7 to 12.9 ng/ml, respectively, and AUC values varied from 16.9 to 83.3 ng.h/ml in adolescents and 20.7 to 66.3 ng.h/ml in adults.

Andre Jackson_____

RD/FT Initialed by Raman Baweja, Ph.D._____

Cc-NDA 20768, HFD-860(Jackson, Baweja), Central Documents Room(Biopharm-CDR)

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/s/

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4/15/04 02:32:12 PM
BIOPHARMACEUTICS

Raman Baweja
4/15/04 05:29:27 PM
BIOPHARMACEUTICS
Memo to File - NDA 20,768, Zolmitriptan Tablets; Adolescents; BPCA Clinical Pharmacology and Biopharmaceutics Summary