2.0 SYNOPSIS

Name of Company: AstraZeneca LP	**Individual Study Table Referring to Item of the Submission** N/A	**(For National Authority Use only)**
Name of Finished Product: NEXIUM	**Volume:** N/A	
Name of Active Ingredient: esomeprazole magnesium	**Page:** N/A	

Title of Study: A Randomized, Open-Label, 2-Period, Crossover Pharmacokinetic Study to Evaluate, After Single and Multiple Doses, Whether Esomeprazole Magnesium (Nexium®) 40 mg Opened Capsule in Water, Administered Through a Nasogastric Tube, is Bioequivalent to an Intact 40 mg Capsule, Administered Orally, in Healthy Subjects

Study Center: 1 investigator site initiated; 1 investigator site enrolled subjects

Publication (reference): None

Studied Period (years): (date of first enrollment) February 10, 2002 (date of last completed) March 22, 2002	**Phase of development:** Phase IV

Objectives:

Primary Objective

1. To evaluate whether esomeprazole 40 mg opened capsule, administered as a dispersion of enteric-coated pellets in water through a nasogastric tube, is bioequivalent to esomeprazole 40 mg administered orally as an intact capsule on Day 1 of dosing.

Secondary Objectives

1. To evaluate whether esomeprazole 40 mg opened capsule, administered as a dispersion of enteric-coated pellets in water through a nasogastric tube on 5 consecutive days, is bioequivalent to esomeprazole 40 mg administered orally as an intact capsule on 5 consecutive days.
2. To assess the safety and tolerability of esomeprazole 40 mg as administered orally and as a dispersion of enteric-coated pellets in water through a nasogastric tube on 5 consecutive days.

Methodology: This was a single-center, randomized, open-label, 2-period crossover study of the pharmacokinetics of NEXIUM (esomeprazole magnesium) in healthy male and female subjects. Subjects were randomized to one of two sequences. Each sequence consisted of two 5-day study periods separated by a 7- to 14-day washout period. The sequences differed only in the order in which subjects participated in the study periods. Subjects remained at the study center for the entire 5 days of each study period, but were allowed to leave during the washout period. Randomization was stratified by gender to ensure equal enrollment of males and females.

During one study period, subjects received a once-daily dose of esomeprazole 40 mg orally as an intact capsule taken with 240 mL of water for 5 consecutive days. In the other study period, subjects received a once-daily dose of esomeprazole 40 mg as an open capsule in water administered through a nasogastric tube for 5 consecutive days. In both study periods, subjects were fasting when they received study drug; a standard breakfast was provided 30 minutes after study drug was taken. Blood samples for pharmacokinetic studies of esomeprazole concentration were obtained up to 12 hours postdose on Days 1 and 5 of each study period.

Number of Patients (Planned and Analyzed): 60 subjects (30 male and 30 female) were randomized. All 60 subjects completed the study.
Number of subjects planned: 40
Number of subjects analyzed: 47 evaluable for Day 1 (primary) and 55 evaluable for Day 5 (secondary)

Diagnosis and Main Criteria for Inclusion: Healthy volunteer between the ages of 18 and 50 years, body weight no more than 20% above or below ideal body weight for height and frame.

Test Product, Dose and Mode of Administration, Batch or Lot Number:
Esomeprazole capsules 40 mg, oral – Lot AM 633.

Duration of Treatment: Two 5-day dosing periods separated by a 7- to 14-day washout period.

Reference Therapy, Dose and Mode of Administration, Batch or Lot Number: None

Name of Company: AstraZeneca LP	**Individual Study Table Referring to Item of the Submission** N/A	**(For National Authority Use only)**
Name of Finished Product: NEXIUM	**Volume:** N/A	
Name of Active Ingredient: esomeprazole magnesium	**Page:** N/A	

Criteria for Evaluation:

Pharmacokinetics: Pharmacokinetic data were analyzed for all evaluable subjects. Evaluable subjects were defined as those subjects who finished both treatment periods with sufficient pharmacokinetic data to determine both an AUC and a C_{max} and who had no major protocol violations or deviations.

Safety: Safety data were summarized for all dosed subjects. Adverse events were documented and vital signs were recorded daily. A physical examination and routine laboratory analyses were performed at screening and at the end of the trial.

Statistical Methods:

Demographic information and safety data were summarized.

AUC and C_{max} were log-transformed prior to analysis. They were analyzed using an analysis of variance (ANOVA) model, fitted for the effects of sequence and subject within sequence, period, and regimen. Contrasts between regimens were calculated, and the results were presented as geometric least squares means (GLS means) of regimen effect (ratio of GLS means of oral versus nasogastric tube) with its 90% confidence interval (90% CI).

t_{max} was summarized using median and range. $t_{1/2}$ was summarized using mean and standard deviation.

SUMMARY

PHARMACOKINETIC RESULTS: The 90% confidence intervals for the ratio of geometric means (NG tube-administered capsule contents/intact capsule) for AUC (0.8693, 1.0806) and C_{max} (0.9320, 1.2475) were within the interval 0.80 to 1.25 on Day 1 of the study. This indicates that the intact capsule administered orally and a dispersion of the capsule contents (enteric-coated pellets) in water administered through a nasogastric (NG) tube are bioequivalent after single dose administration.

The 90% confidence intervals for the ratio of geometric means (NG tube-administered capsule contents/intact capsule) for AUC (0.7922, 0.9712) and C_{max} (0.7899, 0.9705) were just below the lower limit of the interval 0.80 to 1.25 on Day 5 of the study. This indicates that the intact capsule administered orally and a dispersion of the capsule contents (enteric-coated pellets) in water administered through an NG tube have similar bioavailability after 5 consecutive days of dosing.

SAFETY RESULTS: In this study, esomeprazole 40 mg, administered as either an intact capsule or as a dispersion of the capsule contents in water through an NG tube, was generally well-tolerated. There were no deaths, SAEs, or clinically significant laboratory abnormalities or vital sign values.

Date of the Report: September 18, 2002