AstraZeneca

Clinical Study Report Synopsis

Drug Substance	Esomeprazole sodium
Study Code	D9618C00001
Edition Number	1
Date	18 September 2008

A 6-month randomized, double-blind, parallel-group, multicentre, placebo-controlled Phase II study to compare anti-asthmatic effect and safety of esomeprazole (Nexium®) 40 mg twice daily or 40 mg once daily with placebo in adults with asthma

Study dates: First patient enrolled: 03 April 2006
Last patient completed: 23 April 2008

Phase of development: Therapeutic exploratory (II)

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents

Drug product:	NEXIUM®	**SYNOPSIS**	
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Study centre(s)

The study was conducted in 155 sites in 13 countries: Argentina (14 centers), Bulgaria (9 centers), Canada (14 centers), Czech Republic (11 centers), France (9 centers), Germany (16 centers), Hungary (9 centers), Italy (13 centers), Mexico (5 centers), Poland (10 centers), Portugal (5 centers), Slovakia (9 centers), and the United States (31 centers). In addition, 1 patient was enrolled at 1 center in Switzerland; however, this patient was not randomized. Approximately 5 to 15 patients from 14 to 18 countries were proposed.

Publications

None at the time of writing this report.

Study dates		**Phase of development**
First patient enrolled	03 April 2006	Therapeutic exploratory (II)
Last patient completed	23 April 2008	

Objectives

The primary objective of this study was to compare the anti-asthmatic effect of esomeprazole, given either as 40 mg twice daily (E40 bid) or 40 mg once daily (E40 qd), with that of placebo in adult patients with moderate to severe asthma and symptoms of gastroesophageal reflux disease (GERD) by evaluation of change in morning Peak Expiratory Flow (mPEF) from baseline (mean of the last 7 days in the run-in period) to treatment period (mean of all available data during the treatment period) as the primary outcome variable.

The secondary objectives of the study were

- to investigate the effect on symptoms of GERD when treating adult patients having moderate to severe asthma and symptoms of GERD with E40 bid or E40 qd or placebo by evaluation of change in symptoms of GERD as measured by Reflux Disease Questionnaire (RDQ)

- to assess the safety and tolerability of the treatments E40 bid and E40 qd for 6 months.

Study design

This was a 6-month, randomized, double-blind, parallel-group, placebo-controlled, multinational study in patients with sub-optimally controlled moderate to severe asthma and symptoms of GERD. The primary outcome variable was mPEF. This study investigated the anti-asthmatic effect of E40 bid and E40 qd versus placebo in a population with a clear medical need for improved therapy, ie, patients with inhaled glucocorticosteroids (GCSs) and long-acting β_2-agonists (LABAs) as prescribed maintenance therapy for asthma and which were believed to have reflux as a contributing factor to sub-optimal control of their asthma. In accordance with asthma guidelines the treatment period in this study was 6 months.

Target patient population and sample size

Males and females (age 18 to 70 years inclusive) with sub-optimally controlled moderate to severe asthma and symptoms of GERD were enrolled. The patients were to be on inhaled GCSs in combination with LABAs when entering the study and were to remain on this treatment during the study.

Approximately 1800 patients were to be enrolled to obtain approximately 1015 to 1100 adult patients with moderate to severe asthma and symptoms of GERD. Assuming a standard deviation of 40 L/min for the change in mPEF from baseline to treatment period, 338 patients per group were needed in order to have 90% power to detect a difference between groups assuming a true mean difference of 10 L/min. A total of 1513 patients were enrolled, 961 patients were randomized to 1 of the 3 treatment groups, and 828 patients completed the study.

Investigational product and comparator(s): dosage, mode of administration and batch numbers´

Table S1 Details of investigational product and any other study treatments[a]

Investigational product	
Generic name:	esomeprazole
Active ingredient:	esomeprazole magnesium trihydrate
Dosage form:	capsules
Strength:	40 mg/capsule
Formulation number:	H 1222-04-01
No. of capsules/bottle:	40
Manufacturer:	AstraZeneca Tablet Production, Sweden
Batch numbers	H 1222-04-01-15, H 1222-04-01-16
Comparator drug	
Generic name:	placebo for esomeprazole
Active ingredient:	none
Dosage form	capsules
Formulation number:	H 0459-06-03
No. of capsules/bottle:	40
Manufacturer:	AstraZeneca Tablet Production, Sweden
Batch numbers	H 0459-06-03-11, H 0459-06-03-14
Rescue medication	
Generic name:	antacids
Dosage form:	tablets
Acid-binding capacity:	≤16 mmol HCl/tablet
Manufacturer:	to be purchased locally in each country
Medication for reversibility test	
Generic name:	short-acting β_2-agonist
Dosage form:	powder for inhalation/pMDI
Manufacturer:	to be purchased locally in each country

[a] Batch numbers are not required for non-investigational products.

Duration of treatment

In accordance with asthma guidelines, the treatment period in this study was 6 months.

Criteria for evaluation – efficacy (main variables)

The primary objective of this study was to compare the anti-asthmatic effect of E40 bid or E40 qd with that of placebo in adult patients with moderate to severe asthma and symptoms of GERD by evaluation of change in mPEF from baseline (mean of the last 7 days in the run-in period) to treatment period (mean of all available data during the treatment period) as the primary outcome variable.

Furthermore, the anti-asthmatic effect was evaluated by the following secondary outcome variables:

- changes in average value from baseline to treatment period in :
  - evening PEF (ePEF)
  - asthma symptom score - day, night and total
  - number of inhalations of short-acting β_2-agonists (SABAs) - day, night and total
  - percentage of symptom-free days
  - percentage of nights with awakening(s) due to asthma
  - percentage of days free from use of inhaled SABAs
  - percentage of asthma-control days
- changes in forced expiratory volume in 1 second (FEV_1) from randomization (Visit 3) to the mean value at Visits 4-7
- time to first severe asthma exacerbation
- number of severe asthma exacerbations
- change in Asthma Quality of Life Questionnaire, standardized version, (AQLQ(S)) scores (see Appendix D in the CSP) from randomization (Visit 3) to Visit 7
- health-care resource utilization

A secondary objective of this study was to investigate the effect on symptoms of GERD when treating adult patients having moderate to severe asthma and symptoms of GERD with E40 bid or E40 qd or placebo. The change in symptoms of GERD was measured by Reflux Disease Questionnaire (RDQ) from randomization (Visit 3) to Visit 7.

Criteria for evaluation - safety (main variables)

The safety and tolerability of E40 bid and E40 qd for 6 months were assessed by the evaluation of the incidence, severity, and type of adverse events (AEs) and clinical laboratory tests including hematology and clinical chemistry, physical examination, vital signs including blood pressure, pulse rate, and electrocardiogram (ECG).

Statistical methods

The efficacy analyses were based on the Full Analysis Set, as defined in the ICH E9 guideline. Therefore, all randomized patients with any efficacy data available post randomization (the intent-to-treat population [ITT]) were included in the efficacy analyses. The safety analysis set comprised all randomized patients who took at least 1 dose of the investigational product and for whom data was collected post randomization. All safety analyses including AE, safety laboratory evaluation, ECG, vital signs, and physical examinations were performed on the safety analysis set. Patients who were enrolled in the study but not randomized were not included in any analyses.

The primary outcome variable of this study, ie, the change in mPEF from baseline (mean of the last 7 days in the run-in period) to treatment period (mean of all available data during the treatment period), was analyzed using analysis of covariance (ANCOVA) with baseline as a covariate, and treatment and country as factors. Treatment differences were estimated from the model and confidence intervals of 95% confidence level were calculated. All pairwise differences were estimated, ie, E40 bid versus placebo, E40 qd versus placebo, and E40 bid versus E40 qd.

Subject population

In total, 1513 patients were enrolled, 961 patients were randomized, and 828 patients completed the study at 155 study centers in 13 countries. In addition, 1 patient was enrolled at 1 center in Switzerland; however, this patient was not randomized. The first patient was enrolled on 03 April 2006 and the last patient completed the study on 23 April 2008.

Disposition and demographic data of the study population are shown in Table S2. These patients with moderate to severe asthma and symptoms of GERD were predominately female Caucasians, with a mean age of 44 years and mean time to asthma diagnosis of 14 years. The majority of patients were nonsmokers (77%). The treatment groups were balanced with respect to demographic and key baseline characteristics and the demographic and baseline characteristics of the study population were representative of the target patient population.

A total of 828 patients completed the protocol and 133 patients were discontinued from the study. The main reason for discontinuation from the study was incorrect enrollment (67 patients); the second most frequent reason was voluntary discontinuation by the patient (29 patients).

The data from 4 randomized patients were excluded from the ITT analysis because of missing efficacy data after Visit 3 (2 patients), no investigational product administered (1 patient), and

treatment code broken by the investigator (1 patient). The patient who received no investigational product was also excluded from the safety analysis.

Table S2 Patient disposition, demographics, and baseline characteristics[a]

	E40 bid	E40 qd/ Placebo qd	Placebo bid	All
Disposition				
Enrolled patients				1513
Not randomized				552
Incorrect enrollment				434(78.6)
Severe non-compliance to protocol				5(0.9)
Safety reasons				1(0.2)
Adverse event				6(1.1)
Voluntary discontinuation by patient				56(10.1)
Patient lost to follow-up				5(0.9)
Other				45(8.2)
Randomized patients	320	313	328	961
Incorrect enrollment	28(8.8)	19(6.1)	20(6.1)	67(7)
Severe non-compliance to protocol	0(0)	3(1)	0(0)	3(0.3)
Adverse event	4(1.3)	7(2.2)	4(1.2)	15(1.6)
Voluntary discontinuation by patient	10(3.1)	7(2.2)	12(3.7)	29(3)
Patient lost to follow-up	0(0)	2(0.6)	3(0.9)	5(0.5)
Other	6(1.9)	2(0.6)	6(1.8)	14(1.5)
Completed protocol	272(85)	273(87.2)	283(86.3)	828(86.2)
Included in ITT population[b]	318	312	327	957[c]
Included in Safety population[d]	319	313	328	960[e]
Demographic or baseline characteristic				
Country, n (%)				
Argentina	43(13)	42(13)	42(13)	127(13)
Bulgaria	27(8)	29(9)	28(9)	84(9)
Canada	15(5)	14(4)	14(4)	43(4)
Czech rep.	31(10)	30(10)	33(11)	94(10)
France	11(3)	10(3)	9(3)	30(3)
Germany	20(6)	15(5)	22(7)	57(6)
Hungary	15(5)	14(4)	18(6)	47(5)
Italy	9(3)	11(4)	10(3)	30(3)
Mexico	59(18)	59(19)	58(19)	176(18)
Poland	30(9)	33(11)	32(10)	95(10)
Portugal	2(1)	3(1)	2(1)	7(1)
Slovakia	33(10)	28(9)	30(10)	91(9)
US	24(8)	25(8)	30(10)	79(8)

Table S2 Patient disposition, demographics, and baseline characteristics[a]

	E40 bid	E40 qd/ Placebo qd	Placebo bid	All
Gender, n(%)				
Male	79(25)	73(23)	81(26)	233(24)
Female	240(75)	240(77)	247(79)	727(76)
Age (yrs)	44(18-69)	45(19-70)	45(18-70)	44(18-70)
Race, n(%)				
Caucasian	255(80)	249(80)	262(84)	766(80)
Black	6(2)	8(3)	9(3)	23(2)
Other	58(18)	56(18)	57(18)	171(18)
BMI (kg/m^2)	28(18.2-48.7)	28(16-57.4)	28(16-54)	28(16-57.4)
Height (cm)	165 (140-186)	164 (142-189)	165 (146-189)	164 (140-189)
Weight (kg)	76(47-136)	75(41-158)	76(44-147)	76(41-158)
Time to asthma diagnosis (yrs)	13(0.6-61.6)	14(0.5-68.3)	14(0.5-61.8)	14(0.5-68.3)
Smoking status, n (%)				
Non Smoker	245(77)	249(80)	247(79)	741(77)
Ex-Smoker	56(18)	53(17)	75(24)	184(19)
Occasional Smoker	9(3)	6(2)	3(1)	18(2)
Habitual Smoker	9(3)	5(2)	3(1)	17(2)
Packyears (yrs)	5(0-9)	4(1-10)	5(0-20)	5(0-20)
FEV_1 (L)	2.1(0.63-4.38)	2.0(0.68-4.33)	2.0(0.64-4.81)	2.0(0.63-4.81)
FEV_1 (%PN)	65.8 (24.3-97.2)	66 (24.3-137.7)	66.5 (24.3-113.4)	66.1 (24.3-137.7)
FEV_1 reversibility (%)	27.9 (8.1-137.7)	27.3 (8.1-145.8)	26.7 (8.1-121.5)	27.3 (8.1-145.8)
Mean no. of rescue inhalations	2.7(0-12.1)	2.7(0-13.8)	2.6(0-12.3)	2.7(0-13.8)
mPEF (L/min)	288 (112.9-610)	288.1 (100-619.4)	286.4 (103.3-684.3)	287.5 (100-684.3)
Awakenings (% of nights)	57.4(0-100)	58(0-100)	55.6(0-100)	57(0-100)
Asthma symptoms				
Total	2.7(0-5.6)	2.7(0.3-6)	2.6(0.3-6)	2.7(0-6)
Night	1.3(0-3)	1.3(0-3)	1.3(0-3)	1.3(0-3)
Day	1.4(0-2.6)	1.4(0-3)	1.4(0-3)	1.4(0-3)
AQLQ(S)				
Overall score	3.9(1.7-6.8)	3.8(1.5-6.3)	4.0(1.6-6.6)	3.9(1.5-6.8)
Activity limitation	4.1(1.6-7)	3.9(1.4-6.5)	4.1(1.5-6.5)	4.0(1.4-7)
Emotional function	4.0(1-7)	3.9(1-7)	4.2(1.4-7)	4.0(1-7)
Environmental stimuli	3.6(1-7)	3.4(1-7)	3.6(1-7)	3.5(1-7)
Symptoms	3.9(1.8-6.7)	3.8(1.4-6.3)	4.0(1.4-6.7)	3.9(1.4-6.7)

Table S2 Patient disposition, demographics, and baseline characteristics[a]

	E40 bid	E40 qd/ Placebo qd	Placebo bid	All
RDQ				
Dyspepsia	3.8(1-6)	3.8(1-6)	3.7(1-5.8)	3.8(1-6)
GERD dimension	4.1(1.8-6)	4.1(1.9-6)	4.0(2-6)	4.1(1.8-6)
Heartburn	4.0(1-6)	4.1(1-6)	4.0(1-6)	4.0(1-6)
Regurgitation	4.1(1-6)	4.2(1-6)	4.1(1-6)	4.1(1-6)

[a] For categorical data, frequencies are given, for other data mean values and range are given.

[b] Number of randomized patients with any efficacy data available post randomization.

[c] Data from 4 patients were excluded from the ITT efficacy analysis.

[d] Number of randomized patients who took at least 1 dose of the investigational product and for whom data was collected post randomization.

[e] One patient was randomized but did not receive any study treatment.

E40 bid= esomeprazole 40 mg twice daily; E40 qd/Placebo qd = esomeprazole 40 mg once daily, placebo once daily; Placebo bid = placebo twice daily; BMI = body mass index; FEV_1 = Forced expiratory volume in 1 second; FEV_1 (%PN) = Forced expiratory volume in 1 second (%predicted normal); mPEF = morning peak expiratory flow; AQLQ(S) = Asthma Quality of Life Questionnaire, standardized version; RDQ = Reflux Disease Questionnaire.

Summary of efficacy results

The primary outcome variable of this study was the change in mPEF from baseline (mean of the last 7 days in the run-in period) to treatment period (mean of all available data during the treatment period). As shown in Table S3, the greatest adjusted mean change from baseline for mPEF during the treatment period occurred for the E40 bid treatment group (21.19 L/minute). The mean changes for the E40 qd treatment group and the placebo group were 19.18 L/minute and 15.68 L/minute, respectively. As shown in Table S4, the estimated mean difference was greatest for the comparison of E40 bid versus placebo; none of the comparisons, however, was statistically significant.

Table S3 Analysis of effect of esomeprazole treatment on mPEF (L/minute): baseline mean[a], treatment period mean[b], and adjusted mean change from baseline[c] (ITT population, n=957)

Treatment	N	Baseline mean (range)	Treatment period mean (range)	Adjusted mean change
E 40 bid	316	287.0 (113-610)	317 (109-694)	21.1891
E40 qd/placebo qd	311	288.0 (100-619)	315 (113-620)	19.1847
Placebo bid	327	286.0 (103-684)	309 (109-668)	15.6771

[a] Baseline mean defined as mean of the last 7 days in the run-in period.

[b] Treatment period mean defined as mean of all available data during the treatment period.

[c] Analyzed with ANCOVA, with baseline as a covariate and treatment and country as factors.

mPEF = morning peak expiratory flow; E40 bid= esomeprazole 40 mg twice daily; E40 qd/Placebo qd = esomeprazole 40 mg once daily, placebo once daily; Placebo bid = placebo twice daily.

Table S4 Summary of effect of esomeprazole treatment on mPEF (L/minute): estimated mean treatment differences and 95% CIs (ITT population, n=957)

Treatment comparison	N	Estimated mean	95% CI		p-value
			Lower	Upper	
A-B	627	2.0043	-4.7927	8.8014	0.5629
A-C	643	5.5119	-1.1987	12.2226	0.1073
B-C	638	3.5076	-3.2317	10.2469	0.3073

mPEF = morning peak expiratory flow; CIs = confidence intervals; Treatment A = esomeprazole 40 mg twice daily; Treatment B = esomeprazole 40 mg once daily/placebo once daily; Treatment C = placebo twice daily.

Analyzed with ANCOVA, with baseline as a covariate and treatment and country as factors.

There was no significant effect of esomeprazole treatment on asthma symptom score compared to placebo. E40 bid was significantly more effective compared to E40 qd; however, because there was no difference between either dose of esomeprazole when compared to placebo, this result is not clinically relevant.

There was a statistically significant mean difference in FEV_1 between the E40 bid treatment group and placebo group (p=0.0042) for patients in the ITT population. There was a numerical difference between the E40 qd treatment group and the placebo group (p=0.0654).

There were statistically significant differences from randomization to end of treatment in all AQLQ(S) domains and overall for both E40 bid compared to placebo and E40 qd compared to placebo. The maximal estimated mean difference between treatments was 0.4. This is slightly less than minimal important difference (MID), which has been determined to be 0.5.

Based on RDQ scores, both doses of esomeprazole tested significantly reduced the symptoms of GERD compared to placebo.

There were no statistically significant differences between treatment groups for any of the other secondary variables analyzed.

Summary of safety results

As shown in Table S5 and Table S6, E40 bid and E40 qd were well tolerated in this population of adults with asthma. No adverse events with fatal outcome or OAEs occurred during this study. A total of 20 SAEs were reported by 17 patients (1.8%) during the study. None of these SAEs was considered by the investigator to be causally related to study medication. The adverse events reported in this study are consistent with what would be expected in a population of patients with asthma. A total of 15 patients (1.6%) experienced 20 AEs leading to discontinuation during the study. The most commonly reported DAEs occurred in the GI disorders system organ class; these DAEs were reported most frequently by the patients in the E40 qd treatment group and the placebo group (1% each).

Table S5 Number (%) of patients who had at least 1 adverse event in any category and N (%) of total number of adverse events (Safety population)

Category of adverse events	E40 bid (n=319)	E40 qd/ Placebo qd (n=313)	Placebo bid (n=328)	Total (n=960)
	N (%) of patients who had an adverse event in any category[a]			
Any adverse events	115(36.1)	135(43.1)	144(44.0)	394(41.0)
Serious adverse events	7(2.2)	5(1.6)	5(1.5)	17(1.8)
Discontinuation of study treatment due to adverse events	4(1.3)	7(2.2)	4(1.2)	15(1.6)
Related adverse events[b]	9(2.8)	7(2.2)	6(1.8)	22(2.3)
Severe adverse events	3(0.9)	5(1.6)	9(2.7)	17(1.8)
	N (%) of total number of adverse events in any category[c]			
Any adverse events	185(58.0)	205(65.5)	224(68.3)	614(64.0)
Serious adverse events	9(2.8)	5(1.6)	6(1.8)	20(2.1)
Discontinuation of study treatment due to adverse events	5(1.6)	11(3.5)	4(1.2)	20(2.9)
Related adverse events[b]	10(3.1)	11(3.5)	7(2.1)	28(2.9)
Severe adverse events	4(1.3)	5(1.6)	9(2.7)	18(1.9)

[a] Patients with multiple events in the same category are counted only once in that category. Patients with events in more than 1 category are counted once in each of those categories.

[b] Related AEs are those for which there was a possible relationship to investigational product, as judged by the investigator.

[c] Events are counted by preferred term, ie, for patients with multiple events falling under the same preferred term, only 1 occurrence of the event is counted.

E40 bid = esomeprazole 40 mg twice daily; E40 qd/Placebo qd = esomeprazole 40 mg once daily/placebo once daily; Placebo bid = placebo twice daily.

Table S6 Number (%) of patients[a] with the most commonly reported adverse events presented by preferred term in decreasing order of frequency (Safety population)

Preferred term	E40 bid (n=319)	E40 qd/ Placebo qd (n=313	Placebo bid (n=328)	Total (n=960)
Total no. of patients with AE:	**115(36.05)**	**135(43.13)**	**144(43.9)**	**394(41.04)**
Upper respiratory tract infection	26(8.15)	28(8.95)	37(11.28)	91(9.48)
Bronchitis	11(3.45)	16(5.11)	18(5.49)	45(4.69)
Nasopharyngitis	5(1.57)	11(3.51)	16(4.88)	32(3.33)
Pharyngitis	9(2.82)	11(3.51)	7(2.13)	27(2.81)
Asthma	4(1.25)	6(1.92)	10(3.05)	20(2.08)
Headache	8(2.51)	5(1.6)	6(1.83)	19(1.98)
Influenza	8(2.51)	4(1.28)	4(1.22)	16(1.67)
Sinusitis	2(0.63)	9(2.88)	5(1.52)	16(1.67)
Respiratory tract infection	3(0.94)	8(2.56)	3(0.91)	14(1.46)
Viral infection	5(1.57)	7(2.24)	2(0.61)	14(1.46)

Table S6 Number (%) of patients[a] with the most commonly reported adverse events presented by preferred term in decreasing order of frequency (Safety population)

Preferred term	E40 bid (n=319)	E40 qd/ Placebo qd (n=313	Placebo bid (n=328)	Total (n=960)
Hypertension	4(1.25)	7(2.24)	2(0.61)	13(1.35)
Diarrhea	4(1.25)	2(0.64)	4(1.22)	10(1.04)
Gastroenteritis	5(1.57)	3(0.96)	2(0.61)	10(1.04)
Rhinitis allergic	6(1.88)	2(0.64)	2(0.61)	10(1.04)
Nausea	4(1.25)	3(0.96)	2(0.61)	9(0.94)
Abdominal pain	1(0.31)	1(0.32)	5(1.52)	7(0.73)
Rhinitis	4(1.25)	0	3(0.91)	7(0.73)
Flatulence	3(0.94)	2(0.64)	1(0.3)	6(0.63)
Tracheobronchitis	2(0.63)	3(0.96)	1(0.3)	6(0.63)
Vomiting	0	2(0.64)	4(1.22)	6(0.63)
Ear infection	1(0.31)	1(0.32)	3(0.91)	5(0.52)
Pyrexia	1(0.31)	1(0.32)	3(0.91)	5(0.52)
Tonsillitis	0	2(0.64)	3(0.91)	5(0.52)
Acute sinusitis	2(0.63)	1(0.32)	1(0.3)	4(0.42)
Cough	0	1(0.32)	3(0.91)	4(0.42)
Herpes zoster	4(1.25)	0	0	4(0.42)
Laryngitis	1(0.31)	2(0.64)	1(0.3)	4(0.42)
Limb injury	2(0.63)	1(0.32)	1(0.3)	4(0.42)
Nephrolithiasis	1(0.31)	1(0.32)	2(0.61)	4(0.42)
Pruritus	1(0.31)	3(0.96)	0	4(0.42)
Urticaria	0	0	4(1.22)	4(0.42)

[a] This table includes only those events that occurred in at least 4 patients in the Safety population.

Note: AEs presented by preferred term; a patient with multiple events is counted only once within the preferred term.

E40 bid = esomeprazole 40 mg twice daily; E40 qd/Placebo qd = esomeprazole 40 mg once daily/placebo once daily; Placebo bid = placebo twice daily.

The safety data from this study were consistent with the known safety profile of esomeprazole. There were no notable treatment differences for any of the safety variables and no safety concerns were associated with the 6-month use of esomeprazole 40 mg once or twice daily. There was no difference in the safety profile of esomeprazole 40 mg twice daily compared to that of esomeprazole 40 mg once daily.

Date of the report

18 September 2008