



## Clinical trial results:

### A Randomized, Open-Label Study to Evaluate the Pharmacokinetics of Multiple Doses of Esomeprazole Magnesium in a Pediatric Population of 1 to 11 Year olds with Gastroesophageal Reflux Disease (GERD) or Symptoms of GERD

#### Summary

EudraCT number	2012-001157-97
Trial protocol	Outside EU/EEA
Global end of trial date	10 March 2005

#### Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	08 August 2015

#### Trial information

##### Trial identification

Sponsor protocol code	D9614C00099
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	AstraZeneca LP
Sponsor organisation address	1800 Concord Pike, Wilmington, Delaware, United States, 19850
Public contact	AZ Clinical Trial Transparency group, AstraZeneca R&D, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Marta Illueca, MD, FAAP, AstraZeneca LP, 1 302-885-1487,

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000331-PIP01-08
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 March 2005
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 March 2005
Global end of trial reached?	Yes
Global end of trial date	10 March 2005
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To determine the area under the curve (AUC) of esomeprazole after multiple oral doses of 5 mg, 10 mg, and 20 mg esomeprazole magnesium in 1 to 11 year olds, inclusive with GERD or symptoms of GERD.

Protection of trial subjects:

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and that are consistent with ICH/Good Clinical Practice and applicable regulatory requirements and the AstraZeneca policy on Bioethics. The study was approved by the independent Institutional Review Board/Research Ethics Committee, Coast IRB, 901 Calle Amanecer, Suite 260, San Clemente, CA 92673.

Informed consent was obtained from all subjects prior to initiation of the study.

Subjects could be discontinued from study treatment and assessments at any time, voluntary by subject or as judged by the investigator or AstraZeneca.

Background therapy:

The target subject population was male and female children, aged 1 to 11 years inclusive, who suffered from GERD or symptoms of GERD and were candidates for acid suppression therapy.

Eligible subjects had to be able to tolerate discontinuation of their PPI therapy for 7 days and/or H2RA therapy for 3 days prior to the first dose of study drug.

Evidence for comparator:

No comparator group.

Actual start date of recruitment	22 March 2004
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	31
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	2

months)	
Children (2-11 years)	29
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

First subject enrolled: 22 March 2004

Last subject completed: 31 July 2004

### Pre-assignment

Screening details:

34 subjects were screened. Thirty-one (31) of these subjects were randomized and 3 failed screening. Of the 3 screen failures, 1 could not participate due to scheduling conflicts and 2 had abnormal lab values.

### Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open-Label

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Esomeprazole 5 mg (Age 1-5 yr)

Arm description:

Esomeprazole 5 mg (Age 1-5 yr)

Arm type	Experimental
Investigational medicinal product name	Esomeprazole magnesium
Investigational medicinal product code	
Other name	NEXIUM
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

5 mg od orally

<b>Arm title</b>	Esomeprazole 10 mg (Age 1-5 yr)
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Arm description:

Esomeprazole 10 mg (Age 1-5 yr)

Arm type	Experimental
Investigational medicinal product name	Esomeprazole magnesium
Investigational medicinal product code	
Other name	NEXIUM
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg od orally

<b>Arm title</b>	Esomeprazole 10 mg (6-11 years)
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Arm description:

Esomeprazole 10 mg (6-11 years)

Arm type	Experimental
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Investigational medicinal product name	Esomeprazole magnesium
Investigational medicinal product code	
Other name	NEXIUM
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg od orally

<b>Arm title</b>	Esomeprazole 20 mg (6-11 yr)
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Arm description:

Esomeprazole 20 mg (6-11 yr)

Arm type	Experimental
Investigational medicinal product name	Esomeprazole magnesium
Investigational medicinal product code	
Other name	NEXIUM
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

20 mg od orally

<b>Number of subjects in period 1</b>	Esomeprazole 5 mg (Age 1-5 yr)	Esomeprazole 10 mg (Age 1-5 yr)	Esomeprazole 10 mg (6-11 years)
Started	9	9	7
Completed	6	8	7
Not completed	3	1	0
Consent withdrawn by subject	2	1	-
Refused to take study medication on Day 1	1	-	-

<b>Number of subjects in period 1</b>	Esomeprazole 20 mg (6-11 yr)
Started	6
Completed	6
Not completed	0
Consent withdrawn by subject	-
Refused to take study medication on Day 1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Esomeprazole 5 mg (Age 1-5 yr)
Reporting group description:	Esomeprazole 5 mg (Age 1-5 yr)
Reporting group title	Esomeprazole 10 mg (Age 1-5 yr)
Reporting group description:	Esomeprazole 10 mg (Age 1-5 yr)
Reporting group title	Esomeprazole 10 mg (6-11 years)
Reporting group description:	Esomeprazole 10 mg (6-11 years)
Reporting group title	Esomeprazole 20 mg (6-11 yr)
Reporting group description:	Esomeprazole 20 mg (6-11 yr)

Reporting group values	Esomeprazole 5 mg (Age 1-5 yr)	Esomeprazole 10 mg (Age 1-5 yr)	Esomeprazole 10 mg (6-11 years)
Number of subjects	9	9	7
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	2	0
Children (2-11 years)	9	7	7
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Age (years)			
Units: years			
arithmetic mean	3.8	2.3	8.4
full range (min-max)	2 to 5	1 to 4	6 to 11
Gender Categorical			
Units: Subjects			
Female	6	3	2
Male	3	6	5

Reporting group values	Esomeprazole 20 mg (6-11 yr)	Total	
Number of subjects	6	31	
Age Categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	

Infants and toddlers (28 days-23 months)	0	2	
Children (2-11 years)	6	29	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Age (years)			
Units: years			
arithmetic mean	7.8		
full range (min-max)	6 to 11	-	
Gender Categorical			
Units: Subjects			
Female	3	14	
Male	3	17	

### Subject analysis sets

Subject analysis set title	Full data set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Full data set	

Reporting group values	Full data set		
Number of subjects	31		
Age Categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	2		
Children (2-11 years)	29		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Age (years)			
Units: years			
arithmetic mean	5.2		
full range (min-max)	1 to 11		
Gender Categorical			
Units: Subjects			
Female	14		
Male	17		

## End points

### End points reporting groups

Reporting group title	Esomeprazole 5 mg (Age 1-5 yr)
Reporting group description: Esomeprazole 5 mg (Age 1-5 yr)	
Reporting group title	Esomeprazole 10 mg (Age 1-5 yr)
Reporting group description: Esomeprazole 10 mg (Age 1-5 yr)	
Reporting group title	Esomeprazole 10 mg (6-11 years)
Reporting group description: Esomeprazole 10 mg (6-11 years)	
Reporting group title	Esomeprazole 20 mg (6-11 yr)
Reporting group description: Esomeprazole 20 mg (6-11 yr)	
Subject analysis set title	Full data set
Subject analysis set type	Intention-to-treat
Subject analysis set description: Full data set	

### Primary: Primary PK parameter AUC

End point title	Primary PK parameter AUC <sup>[1]</sup>
End point description: AUC after repeated doses	
End point type	Primary
End point timeframe: after repeated doses (5 days)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive - No statistical analyses were specified for this primary end point

End point values	Esomeprazole 5 mg (Age 1-5 yr)	Esomeprazole 10 mg (Age 1- 5 yr)	Esomeprazole 10 mg (6-11 years)	Esomeprazole 20 mg (6-11 yr)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5 <sup>[2]</sup>	8 <sup>[3]</sup>	7 <sup>[4]</sup>	6 <sup>[5]</sup>
Units: micromol*h/L				
geometric mean (standard deviation)	0.74 (± 0.36)	4.83 (± 2.56)	3.7 (± 2.05)	6.28 (± 2.71)

Notes:

[2] - number of subjects evaluated for AUC

[3] - number of subjects evaluated for AUC

[4] - number of subjects evaluated for AUC

[5] - number of subjects evaluated for AUC

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment (5 days)

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	6.0
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### Reporting groups

Reporting group title	Esomeprazole 5 mg (Age 1-5 yr)
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Reporting group description:

Esomeprazole 5 mg (Age 1-5 yr)

Reporting group title	Esomeprazole 10 mg (Age 1-5 yr)
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Reporting group description:

Esomeprazole 10 mg (Age 1-5 yr)

Reporting group title	Esomeprazole 10 mg (6-11 years)
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Reporting group description:

Esomeprazole 10 mg (6-11 years)

Reporting group title	Esomeprazole 20 mg (6-11 yr)
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Reporting group description:

Esomeprazole 20 mg (6-11 yr)

Serious adverse events	Esomeprazole 5 mg (Age 1-5 yr)	Esomeprazole 10 mg (Age 1-5 yr)	Esomeprazole 10 mg (6-11 years)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Esomeprazole 20 mg (6-11 yr)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Injury, poisoning and procedural complications			
Skin laceration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

<b>Non-serious adverse events</b>	Esomeprazole 5 mg (Age 1-5 yr)	Esomeprazole 10 mg (Age 1-5 yr)	Esomeprazole 10 mg (6-11 years)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 7 (0.00%)
Injury, poisoning and procedural complications			
Excoriation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Faeces discoloured			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 7 (0.00%)
occurrences (all)	0	2	0

<b>Non-serious adverse events</b>	Esomeprazole 20 mg (6-11 yr)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)		
Injury, poisoning and procedural complications			
Excoriation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported