



## Clinical trial results:

### A Multicenter, Open label, Non-comparative Study to Evaluate the Safety of Entocort EC for the Treatment of Crohn's Disease in Paediatric Subjects Aged 5 to 17 Years, Inclusive

#### Summary

EudraCT number	2011-003743-22
Trial protocol	DE IT
Global end of trial date	10 September 2014

#### Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	13 May 2015

#### Trial information

##### Trial identification

Sponsor protocol code	D9422C00001
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01444092
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	AstraZeneca R&D Mölndal
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Notes:

##### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 September 2014
Global end of trial reached?	Yes
Global end of trial date	10 September 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate the safety of Entocort EC in a pediatric population treated for mild-to-moderate Crohn's disease

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 November 2011
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	Poland: 40
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United States: 47
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Canada: 19
Worldwide total number of subjects	123
EEA total number of subjects	57

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 months)	0
Children (2-11 years)	23
Adolescents (12-17 years)	100
Adults (18-64 years)	0
From 65 to 84 years	0



## Subject disposition

### Recruitment

Recruitment details:

This study was to enroll approximately 110 subjects at study centers in the United States and at multiple centers throughout Europe and Canada.

### Pre-assignment

Screening details:

Eligibility for study enrollment will be assessed at the screening and enrollment visit (Visit 1). If appropriate, subjects will be enrolled into the study and begin to receive study medication at this visit. 123 subjects were screened and 108 were enrolled.

### Period 1

Period 1 title	Enrollment/screening/start of treatment
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

<b>Arm title</b>	Entocort
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Entocort EC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

9 or 6 mg once daily in the morning

<b>Number of subjects in period 1<sup>[1]</sup></b>	Entocort
Started	108
Completed	108

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of 123 enrolled patients under Trial information only 108 were treated. 15 patients were enrolled but not treated (did not meet the criteria for entering).

### Period 2

Period 2 title	Overall study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

<b>Arm title</b>	Entocort
Arm description: Entocort EC 9 or 6 mg/day	
Arm type	Experimental
Investigational medicinal product name	Entocort EC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:  
9 or 6 mg once daily in the morning

<b>Number of subjects in period 2</b>	Entocort
Started	108
Completed	91
Not completed	17
Consent withdrawn by subject	1
Study-specific criterion	1
Adverse event, non-fatal	8
Protocol deviation	1
Lack of efficacy	6

## Baseline characteristics

### Reporting groups

Reporting group title	Entocort
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Reporting group description: -

Reporting group values	Entocort	Total	
Number of subjects	108	108	
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	0	
Children (2-11 years)	18	18	
Adolescents (12-17 years)	90	90	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	13.7		
standard deviation	± 2.4	-	
Gender, Male/Female			
Units: Participants			
Female	51	51	
Male	57	57	
Age, Customized			
Units: Subjects			
=<8 Yrs	5	5	
>8 Yrs	103	103	
Race, Customized			
Units: Subjects			
Asian	1	1	
Black Or African American	4	4	
Other	3	3	
White	100	100	

## End points

### End points reporting groups

Reporting group title	Entocort
Reporting group description: -	
Reporting group title	Entocort
Reporting group description: Entocort EC 9 or 6 mg/day	

### Primary: Any adverse event

End point title	Any adverse event <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe: 12 weeks	

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: Detailed information about the adverse events is to be found in the Adverse events section.

End point values	Entocort			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: Patients	79			

### Statistical analyses

No statistical analyses for this end point

### Secondary: PCDAI

End point title	PCDAI
End point description: Paediatric Crohn's Disease Activity Index	
End point type	Secondary
End point timeframe: 8 weeks	

<b>End point values</b>	Entocort			
Subject group type	Reporting group			
Number of subjects analysed	105 <sup>[2]</sup>			
Units: Score				
arithmetic mean (standard deviation)				
Baseline (Day1)	19.1 (± 10.1)			
Change after 8 weeks	-10 (± 10.1)			

Notes:

[2] - Full analysis set (all patients with a PCDAI after 8 weeks)

### Statistical analyses

No statistical analyses for this end point

### Secondary: IMPACT 3

End point title	IMPACT 3
End point description:	
End point type	Secondary
End point timeframe:	
8 weeks	

<b>End point values</b>	Entocort			
Subject group type	Reporting group			
Number of subjects analysed	107			
Units: Score				
arithmetic mean (standard deviation)				
Baseline (Day 1)	132.1 (± 18.8)			
Change after 8 weeks	7.9 (± 13.3)			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

12 weeks

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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### Reporting groups

Reporting group title	Entocort
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Reporting group description:

Entocort™ EC 9/6/3 mg

<b>Serious adverse events</b>	Entocort		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 108 (7.41%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	4 / 108 (3.70%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema nodosum			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	Entocort		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 108 (72.22%)		
Vascular disorders			
Pallor			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Tenderness			

subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Reproductive system and breast disorders			
Menstrual disorder subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Dysmenorrhoea subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Metrorrhagia subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	3 / 108 (2.78%) 3		
Respiratory tract congestion subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Psychiatric disorders			
Affect lability subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Agitation subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Anxiety subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Depression subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Insomnia subjects affected / exposed occurrences (all)	6 / 108 (5.56%) 6		
Irritability			

subjects affected / exposed occurrences (all)	14 / 108 (12.96%) 14		
Sleep disorder subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Mood swings subjects affected / exposed occurrences (all)	3 / 108 (2.78%) 3		
Investigations			
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Blood albumin decreased subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Blood cortisol decreased subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Blood cortisol increased subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Haemoglobin decreased subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
C-reactive protein increased subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Mean cell volume decreased subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Occult blood positive subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Protein urine present			

<p>subjects affected / exposed occurrences (all)</p> <p>Red blood cell sedimentation rate increased</p> <p>subjects affected / exposed occurrences (all)</p> <p>Urine output decreased</p> <p>subjects affected / exposed occurrences (all)</p>	<p>1 / 108 (0.93%) 1</p> <p>3 / 108 (2.78%) 3</p> <p>1 / 108 (0.93%) 1</p>		
<p>Injury, poisoning and procedural complications</p> <p>Concussion</p> <p>subjects affected / exposed occurrences (all)</p> <p>Incision site complication</p> <p>subjects affected / exposed occurrences (all)</p> <p>Contusion</p> <p>subjects affected / exposed occurrences (all)</p> <p>Procedural pain</p> <p>subjects affected / exposed occurrences (all)</p>	<p>1 / 108 (0.93%) 1</p> <p>1 / 108 (0.93%) 1</p> <p>1 / 108 (0.93%) 1</p> <p>1 / 108 (0.93%) 1</p>		
<p>Cardiac disorders</p> <p>Tachycardia</p> <p>subjects affected / exposed occurrences (all)</p>	<p>2 / 108 (1.85%) 2</p>		
<p>Nervous system disorders</p> <p>Disturbance in attention</p> <p>subjects affected / exposed occurrences (all)</p> <p>Dizziness</p> <p>subjects affected / exposed occurrences (all)</p> <p>Headache</p> <p>subjects affected / exposed occurrences (all)</p> <p>Lethargy</p>	<p>3 / 108 (2.78%) 3</p> <p>1 / 108 (0.93%) 1</p> <p>9 / 108 (8.33%) 9</p>		

<p>subjects affected / exposed occurrences (all)</p> <p>Memory impairment subjects affected / exposed occurrences (all)</p> <p>Migraine subjects affected / exposed occurrences (all)</p> <p>Psychomotor hyperactivity subjects affected / exposed occurrences (all)</p> <p>Syncope subjects affected / exposed occurrences (all)</p>	<p>1 / 108 (0.93%) 1</p> <p>4 / 108 (3.70%) 4</p> <p>1 / 108 (0.93%) 1</p> <p>1 / 108 (0.93%) 1</p> <p>1 / 108 (0.93%) 1</p>		
<p>Blood and lymphatic system disorders</p> <p>Anaemia subjects affected / exposed occurrences (all)</p> <p>Increased tendency to bruise subjects affected / exposed occurrences (all)</p> <p>Lymphadenopathy subjects affected / exposed occurrences (all)</p>	<p>5 / 108 (4.63%) 5</p> <p>1 / 108 (0.93%) 1</p> <p>1 / 108 (0.93%) 1</p>		
<p>Eye disorders</p> <p>Iritis subjects affected / exposed occurrences (all)</p> <p>Scleritis subjects affected / exposed occurrences (all)</p>	<p>1 / 108 (0.93%) 1</p> <p>1 / 108 (0.93%) 1</p>		
<p>Gastrointestinal disorders</p> <p>Abdominal distension subjects affected / exposed occurrences (all)</p> <p>Abdominal pain</p>	<p>1 / 108 (0.93%) 1</p>		

subjects affected / exposed	16 / 108 (14.81%)		
occurrences (all)	16		
Abdominal mass			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Abdominal pain lower			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Abdominal tenderness			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Anal fissure			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Anal haemorrhage			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Anal skin tags			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Breath odour			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Cheilosis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Crohn's disease			
subjects affected / exposed	7 / 108 (6.48%)		
occurrences (all)	7		
Diarrhoea			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Dyspepsia			

subjects affected / exposed occurrences (all)	3 / 108 (2.78%) 3		
Enterocolitis subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Haematochezia subjects affected / exposed occurrences (all)	3 / 108 (2.78%) 3		
Proctalgia subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Nausea subjects affected / exposed occurrences (all)	6 / 108 (5.56%) 6		
Rectal haemorrhage subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Vomiting subjects affected / exposed occurrences (all)	5 / 108 (4.63%) 5		
<b>Skin and subcutaneous tissue disorders</b>			
Alopecia subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Acne subjects affected / exposed occurrences (all)	15 / 108 (13.89%) 15		
Dry skin subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Erythema nodosum subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Hair growth abnormal subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		

Hirsutism			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Lipohypertrophy			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Skin striae			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	13 / 108 (12.04%)		
occurrences (all)	13		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Fistula			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		
Musculoskeletal discomfort			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		

Musculoskeletal pain subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Myalgia subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Osteoporosis subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Pain in extremity subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Infections and infestations			
Acarodermatitis subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Conjunctivitis subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Enteritis infectious subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Gastroenteritis subjects affected / exposed occurrences (all)	2 / 108 (1.85%) 2		
Otitis externa subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 108 (3.70%) 4		
Pharyngitis subjects affected / exposed occurrences (all)	4 / 108 (3.70%) 4		
Rhinitis			

subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Rectal abscess subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Tooth abscess subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 108 (2.78%) 3		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Viral infection subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Viral pharyngitis subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
<b>Metabolism and nutrition disorders</b>			
Decreased appetite subjects affected / exposed occurrences (all)	6 / 108 (5.56%) 6		
Dehydration subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Hyperamylasaemia subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Hyperphagia subjects affected / exposed occurrences (all)	1 / 108 (0.93%) 1		
Increased appetite subjects affected / exposed occurrences (all)	17 / 108 (15.74%) 17		



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 May 2013	The body weight cutoff for 9 mg or 6 mg/day was changed from 30 kg to 25 kg

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported