Clinical trial results:
A Multi-Center, Randomized, Double Blind, Placebo Controlled Parallel Group Study of the Safety of Levocetirizine Dihydrochloride Oral Liquid Formulation b.i.d Dosing in Children Aged 1 to < 6 Years Suffering From Allergic Rhinitis or Chronic Urticaria of Unknown Origin

Summary

EudraCT number	2015-000205-39
Trial protocol	Outside EU/EEA
Global end of trial date	08 July 2008

Results information

Result version number	v1 (current)
This version publication date	28 June 2016
First version publication date	03 May 2015

Trial information

Trial identification

Sponsor protocol code	A00426

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00619801
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Pharma
Sponsor organisation address	1950 Lake Park Drive, Smyrna, United States, 30080
Public contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 15, clinicaltrials@ucb.com
Scientific contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 15, clinicaltrials@ucb.com

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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 August 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 July 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years.

Protection of trial subjects:

Adequate information was provided to the subject's caregiver in both oral and written form and consent was obtained in writing prior to performance of any study specific procedure. The content and process of obtaining informed consent was in accordance with all applicable regulatory and IEC/IRB requirements. A HIPAA agreement was inserted into the final informed consent form for sites in the United States.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	13 March 2008
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: 173
Worldwide total number of subjects	173
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 months)	25
Children (2-11 years)	148
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:

A00426 began recruitment within the United States of America in March 2008. The study concluded in July 2008. A total of 173 were randomized into the study.

Pre-assignment

Screening details:

N/A

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo (5 drops) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

Placebo oral drops (5 drops) dosed twice a day for 2 weeks.

Arm title	Levocetirizine

Arm description:

Levocetirizine dihydrochloride 1.25 mg (5 drops containing 5 mg/mL) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

Arm type	Experimental
Investigational medicinal product name	Levocetirizine
Investigational medicinal product code	Levocetirizine
Other name	Xyzal
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

Levocetirizine dihydrochloride 1.25 mg oral drops formulation (5 drops containing 5mg/mL) dosed twice a day for 2 weeks.

Number of subjects in period 1	Placebo	Levocetirizine
Started	59	114
Safety Population	59	114
Completed	58	111
Not completed	1	3
Consent withdrawn by subject	1	1
Loss of efficacy	-	1
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo (5 drops) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).	
Reporting group title	Levocetirizine
Reporting group description:	
Levocetirizine dihydrochloride 1.25 mg (5 drops containing 5 mg/mL) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).	

Reporting group values	Placebo	Levocetirizine	Total
Number of subjects	59	114	173
Age Categorical Units: Subjects			
<=18 years	59	114	173
Age Continuous Units: years			
arithmetic mean	3.75	3.78	
standard deviation	± 1.45	± 1.38	-
Gender Categorical Units: Subjects			
Female	23	49	72
Male	36	65	101
Region of Enrollment Units: Subjects			
United States	59	114	173

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo (5 drops) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

Reporting group title	Levocetirizine

Reporting group description:

Levocetirizine dihydrochloride 1.25 mg (5 drops containing 5 mg/mL) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in ventricular rate (VR)

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in ventricular rate (VR)[1]

End point description:

End point type	Primary

End point timeframe:

Baseline, 14 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	110		
Units: beats per minute				
arithmetic mean (standard deviation)				
mean (standard deviation)	-1.5 (± 14.1)	1.3 (± 14.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in RR interval

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in RR interval[2]

End point description:

The RR interval refers to the respective time interval in the Electrocardiogram (ECG).

End point type	Primary

End point timeframe:

Baseline, 14 days

Notes:

[2] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56[3]	110[4]		
Units: milliseconds				
arithmetic mean (standard deviation)				
mean (standard deviation)	9.2 (± 85.9)	-6.9 (± 83.4)		

Notes:

[3] - Safety Population; only non-missing values were analyzed.

[4] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in PR interval

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in PR interval[5]

End point description:

The PR interval refers to the respective time interval in the Electrocardiogram (ECG).

End point type	Primary

End point timeframe:

Baseline, 14 days

Notes:

[5] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56[6]	110[7]		
Units: milliseconds				
arithmetic mean (standard deviation)				
mean (standard deviation)	0.5 (± 9.6)	-0.8 (± 11)		

Notes:

[6] - Safety Population; only non-missing values were analyzed.

[7] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QRS duration

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QRS duration[8]

End point description:

The QRS duration refers to the respective time duration in the Electrocardiogram (ECG).

End point type	Primary

End point timeframe:

Baseline, 14 days

Notes:

[8] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56[9]	110[10]		
Units: milliseconds				
arithmetic mean (standard deviation)				
mean (standard deviation)	0.3 (± 6.6)	0.9 (± 7.1)		

Notes:

[9] - Safety Population; only non-missing values were analyzed.

[10] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QT interval

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QT interval[11]

End point description:

The QT interval refers to the respective time interval in the Electrocardiogram (ECG).

End point type	Primary

End point timeframe:

Baseline, 14 days

Notes:

[11] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56[12]	110[13]		
Units: milliseconds				
arithmetic mean (standard deviation)				
mean (standard deviation)	-2.8 (± 17.2)	-1.5 (± 19.2)		

Notes:

[12] - Safety Population; only non-missing values were analyzed.

[13] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QT interval corrected for heart rate using Fridericia's formula (QTcF)

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in QT interval corrected for heart rate using Fridericia's formula (QTcF)[14]

End point description:

The QT interval refers to the respective time interval in the Electrocardiogram (ECG).

End point type	Primary

End point timeframe:

Baseline, 14 days

Notes:

[14] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56[15]	110[16]		
Units: milliseconds				
arithmetic mean (standard deviation)				
mean (standard deviation)	-5.5 (± 14.3)	-0.3 (± 16.6)		

Notes:

[15] - Safety Population; only non-missing values were analyzed.

[16] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Absolute value of QT interval corrected for heart rate using Fridericia's formula (QTcF) at Visit 3 (Day 7)

End point title	Absolute value of QT interval corrected for heart rate using Fridericia's formula (QTcF) at Visit 3 (Day 7)[17]

End point description:

The QT interval refers to the respective time interval in the Electrocardiogram (ECG).

End point type	Primary

End point timeframe:

7 days

Notes:

[17] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[18]	112[19]		
Units: milliseconds				
arithmetic mean (standard deviation)				
mean (standard deviation)	372.6 (± 16.5)	368.9 (± 19.4)		

Notes:

[18] - Safety Population; only non-missing values were analyzed.

[19] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Absolute value of QT interval corrected for heart rate using Fridericia's formula (QTcF) at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV)

End point title	Absolute value of QT interval corrected for heart rate using Fridericia's formula (QTcF) at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV)[20]

End point description:

The QT interval refers to the respective time interval in the Electrocardiogram (ECG).

End point type	Primary

End point timeframe:

14 days

Notes:

[20] - 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: The primary objective of study A00426 was "to evaluate the safety of levocetirizine dihydrochloride in pediatric subjects aged from 1 to less than 6 years". So the purpose of the study was the description of the safety profile of levocetirizine dihydrochloride across several safety variables. Therefore no statistical comparisons were applied in this safety study.

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57[21]	111[22]		
Units: milliseconds				
arithmetic mean (standard deviation)				
mean (standard deviation)	369.8 (± 17.1)	370.5 (± 18.5)		

Notes:

[21] - Safety Population; only non-missing values were analyzed.

[22] - Safety Population; only non-missing values were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation

Visit (EDV) in total bilirubin

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in total bilirubin

End point description:

End point type	Secondary

End point timeframe:

Baseline, 14 days

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	104		
Units: micromole per liter [µmol/L]				
median (full range (min-max))				
median (full range)	0 (-10.26 to 3.42)	0 (-8.55 to 5.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in alanine aminotransferase (ALT)

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in alanine aminotransferase (ALT)

End point description:

End point type	Secondary

End point timeframe:

Baseline, 14 days

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	105		
Units: unit per liter [U/L]				
median (full range (min-max))				
median (full range)	-1.5 (-12 to 167)	1 (-21 to 138)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in aspartate aminotransferase (AST)

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in aspartate aminotransferase (AST)

End point description:

End point type	Secondary

End point timeframe:

Baseline, 14 days

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	105		
Units: unit per liter [U/L]				
median (full range (min-max))				
median (full range)	1 (-15 to 52)	1 (-16 to 58)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in blood urea nitrogen

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in blood urea nitrogen

End point description:

End point type	Secondary

End point timeframe:

Baseline, 14 days

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	105		
Units: millimole per liter [mmol/L]				
median (full range (min-max))				
median (full range)	-0.1785 (-2.142 to 2.142)	0 (-3.57 to 3.213)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in blood creatinine

End point title	Change from baseline at Visit 4 (Day 14) or at Early Discontinuation Visit (EDV) in blood creatinine

End point description:

End point type	Secondary

End point timeframe:

Baseline, 14 days

End point values	Placebo	Levocetirizine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	105		
Units: micromole per liter [µmol/L]				
median (full range (min-max))				
median (full range)	-0.884 (-17.68 to 13.26)	1.768 (-15.912 to 16.796)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from Visit 1 (Day -2 to -28) over randomization and On-treatment Period up to the Follow-up Visit (Day 21±2).

Adverse event reporting additional description:

Adverse Events refer to the safety population, including all subjects who were dispensed study treatment at least once.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Levocetirizine

Reporting group description:

Levocetirizine dihydrochloride 1.25 mg (5 drops containing 5 mg/mL) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

Reporting group title	Placebo

Reporting group description:

Placebo (5 drops) dosed by mouth at breakfast time and in the evening (the evening dose should be administered approximately 12 hours later), twice a day for 2 weeks from Visit 2 (Day 0) to Visit 4 (Day 14) or the Early Discontinuation Visit (EDV).

Serious adverse events	Levocetirizine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Pyrexia			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Levocetirizine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 114 (34.21%)	21 / 59 (35.59%)	
General disorders and administration site conditions			
Pyrexia			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	5 / 114 (4.39%)	1 / 59 (1.69%)	
occurrences (all)	5	1	
Fatigue			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Pain			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Hunger			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Thirst			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	4 / 114 (3.51%)	5 / 59 (8.47%)	
occurrences (all)	4	6	
Asthma			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Wheezing			
alternative dictionary used: MedDRA 9.0			

subjects affected / exposed	1 / 114 (0.88%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Epistaxis			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	2 / 114 (1.75%)	1 / 59 (1.69%)	
occurrences (all)	2	1	
Nasal discomfort			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Respiratory tract congestion			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Psychiatric disorders			
Sleep disorder			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	2 / 114 (1.75%)	0 / 59 (0.00%)	
occurrences (all)	2	0	
Nervousness			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Middle insomnia			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Restlessness			
alternative dictionary used: MedDRA 9.0			

subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Skin laceration			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Head injury			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Tachycardia			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Somnolence			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	2 / 59 (3.39%)	
occurrences (all)	1	2	
Headache			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Psychomotor hyperactivity			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	3 / 59 (5.08%)	
occurrences (all)	0	3	
Ear and labyrinth disorders			

Cerumen impaction			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Eye disorders			
Eye swelling			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	4 / 114 (3.51%)	2 / 59 (3.39%)	
occurrences (all)	4	2	
Vomiting			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	4 / 114 (3.51%)	2 / 59 (3.39%)	
occurrences (all)	4	2	
Teething			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Eructation			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Constipation			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Salivary hypersecretion			

alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Aphthous stomatitis			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Scab			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Dermatitis diaper			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Swelling face			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Skin irritation			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Rash			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	2	0	
Urticaria			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Rash papular			
alternative dictionary used: MedDRA 9.0			

subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Infections and infestations			
Upper respiratory tract infection			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	3 / 114 (2.63%)	2 / 59 (3.39%)	
occurrences (all)	3	2	
Nasopharyngitis			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	2 / 59 (3.39%)	
occurrences (all)	1	2	
Otitis media			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	3 / 114 (2.63%)	0 / 59 (0.00%)	
occurrences (all)	3	0	
Gastroenteritis viral			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	1 / 59 (1.69%)	
occurrences (all)	1	1	
Viral rash			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
alternative dictionary used: MedDRA 9.0			

subjects affected / exposed	1 / 114 (0.88%)	2 / 59 (3.39%)	
occurrences (all)	1	2	
Viral pharyngitis			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Gastroenteritis			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	2 / 114 (1.75%)	0 / 59 (0.00%)	
occurrences (all)	2	0	
Folliculitis			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Hordeolum			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	1 / 114 (0.88%)	0 / 59 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Anorexia			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	
Dehydration			
alternative dictionary used: MedDRA 9.0			
subjects affected / exposed	0 / 114 (0.00%)	1 / 59 (1.69%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 February 2008	The protocol was amended to incorporate changes based on comments received by the Food and Drug Administration to the pre-IND file dated 14 November 2007. Efficacy assessments and serum drug concentration to assess compliance/ drug exposure were incorporated. Children aged 1 but less than 2 years were added to the inclusion criteria. The upper age for inclusion was clarified for children to less than 6 years of age. Information regarding pharmacokinetic modeling to predict dosing regimen in children less than 6 was added.
28 March 2008	The protocol was amended primarily to revise the exclusion criteria to require the specified washout period for subjects who are receiving exclusionary medications via breast milk during the course of the study. The laboratory texts exclusion criteria was amended to clarify that prior written approval from the UCB Clinical Research Physician for out of range laboratory tests in not required before enrolling a subject in the study. The decision to enroll such a subject was left up to the discretion of the Investigator. The prohibited concomitant medications exclusion criterion was amended to clarify that subjects taking single ingredient guaifenesin products at the time of study entry will not be required to perform the wash-out period, and that is the only cough or cold medication that subjects were allowed to take during the study period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported