Clinical trial results:
Double-blind, double-dummy, multi-center, randomized parallel group study to demonstrate therapeutic equivalence of Salmeterol/Fluticasone DPI HEXAL versus SeretideTM 100 AccuhalerTM over a period of 12 weeks in pediatric patients with persistent moderate asthma

Summary

EudraCT number	2007-005630-36
Trial protocol	LT PL
Global end of trial date	22 February 2010

Results information

Result version number	v2 (current)
This version publication date	24 March 2016
First version publication date	05 August 2015
Version creation reason	• Correction of full data set Information about articel 46 was wrong

Trial information

Trial identification

Sponsor protocol code	2006-57-DPI-2

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	HEXAL AG
Sponsor organisation address	Industriestraße 25, Holzkirchen, Germany, 83607
Public contact	Head of Clinical Research Department, Hexal AG, 0049 80249080,
Scientific contact	Head of Clinical Research Department, Hexal AG, 0049 80249080,

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 November 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 February 2010
Global end of trial reached?	Yes
Global end of trial date	22 February 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to evaluate the long-term efficacy and safety of Salmeterol/Fluticasone DPI HEXAL compared to SeretideTM 100 AccuhalerTM in pediatric patients suffering from persistent moderate asthma.

Protection of trial subjects:

Safety assessments included adverse events (AEs), physical examination, ECG, vital signs and clinical laboratory data. This study was conducted in accordance with International Conference on Harmonisation of Good Clinical Practice, the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements.

Background therapy:

-

Evidence for comparator: -

Actual start date of recruitment	22 July 2009
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	Lithuania: 34
Country: Number of subjects enrolled	Poland: 71
Country: Number of subjects enrolled	Romania: 13
Country: Number of subjects enrolled	Ukraine: 100
Worldwide total number of subjects	218
EEA total number of subjects	118

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)	218

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:

Double-blind, double-dummy, multi-center, randomized, parallel group study in pediatric patients with persistent moderate asthma.

Pre-assignment

Screening details:

A total number of 229 patients where screened and 218 patients were randomized. The study consisted of a 2-week run-in wash-out period and a 12-week blinded treatment period. A screening visit (Visit -1) was followed by a 2-week run-in wash-out period during which all asthma treatments except reliever medication were to be stopped.

Pre-assignment period milestones

Number of subjects started	229[1]
Number of subjects completed	218

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Ineligibility: 8
Reason: Number of subjects	Other reason: 1
Reason: Number of subjects	Consent withdrawn by subject: 2

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 11 Patients dropped out according to protocol.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Salmeterol/Fluticasone DPI HEXAL

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Salmeterol/Fluticasone DPI HEXAL
Investigational medicinal product code	
Other name	NA
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

Salmeterol/Fluticasone DPI HEXAL (50 µg salmeterol/100 µg fluticasone per actuation), one actuation two times per day

Arm title	Seretide 100 Accuhaler

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	Seretide 100 Accuhaler
Investigational medicinal product code	
Other name	NA
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

Seretide 100 Accuhaler (50 µg salmeterol/100 µg fluticasone per actuation), one actuation two times per day

Number of subjects in period 1	Salmeterol/Fluticasone DPI HEXAL	Seretide 100 Accuhaler
Started	110	108
Completed	108	106
Not completed	2	2
Consent withdrawn by subject	1	1
Lost to follow-up	1	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Salmeterol/Fluticasone DPI HEXAL
Reporting group description: -	
Reporting group title	Seretide 100 Accuhaler
Reporting group description: -	

Reporting group values	Salmeterol/Fluticasone DPI HEXAL	Seretide 100 Accuhaler	Total
Number of subjects	110	108	218
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0	0	0
Preterm newborn- gestational age < 37 wk	0	0	0
Newborns (0-27days)	0	0	0
Infants and toddlers (28days – 23months)	0	0	0
Children (2-11 years)	110	108	218
Adolescents (12-17 year)	0	0	0
From 18 - 64 years	0	0	0
From 65 – 84 years	0	0	0
Over 85 years	0	0	0
Age Continuous			
Age Continuous Characteristic			
Units: Years			
arithmetic mean	8.1	8.5	
standard deviation	± 2	± 1.8	-
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	38	39	77
Male	72	69	141

End points

End points reporting groups

Reporting group title	Salmeterol/Fluticasone DPI HEXAL
Reporting group description: -	
Reporting group title	Seretide 100 Accuhaler
Reporting group description: -	
Subject analysis set title	Salmeterol/Fluticasone DPI HEXAL (6-11 years) - Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The analysis set consists of all patients who were randomized and received at least one dose of IP.	
Subject analysis set title	Seretide 100 Accuhaler (4-5 years) - Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The analysis set consists of all patients who were randomized and received at least one dose of IP.	
Subject analysis set title	Salmeterol/Fluticasone DPI HEXAL (4-5 years) - Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The analysis set consists of all patients who were randomized and received at least one dose of IP.	
Subject analysis set title	Seretide 100 Accuhaler (4-5 years) - FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The analysis set consists of all patients who were included in the Safety Set and had clinic FEV1 data after the baseline visit.	
Subject analysis set title	Salmeterol/Fluticasone DPI HEXAL (6-11 years) - FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The analysis set consists of all patients who were included in the Safety Set and had clinic FEV1 data after the baseline visit.	
Subject analysis set title	Seretide 100 Accuhaler (6-11 years) - Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The analysis set consists of all patients who were randomized and received at least one dose of IP.	
Subject analysis set title	Salmeterol/Fluticasone DPI HEXAL (4-5 years) - FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The analysis set consists of all patients who were included in the SS and had clinic FEV1 data after the baseline visit.	
Subject analysis set title	Salmeterol/Fluticasone DPI HEXAL (6-11 years) - PPS
Subject analysis set type	Per protocol
Subject analysis set description:	
The analysis set consists of all patients who were included in the FAS and completed the study and had no major protocol violations.	
Subject analysis set title	Seretide 100 Accuhaler (6-11 years) - FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
The analysis set consists of all patients who were included in the Safety Set and had clinic FEV1 data after the baseline visit.	
Subject analysis set title	Seretide 100 Accuhaler (6-11 years) - PPS
Subject analysis set type	Per protocol
Subject analysis set description:	
The analysis set consists of all patients who were included in the FAS and completed the study and had	

no major protocol violations.

Primary: Relative Change in FEV1 from baseline to the end of treatment period	
End point title	Relative Change in FEV1 from baseline to the end of treatment period

End point description:

The change in FEV1 from baseline at the end of the 12-
week treatment period. Missing values of the primary endpoint 'relative change in FEV1' were replaced using the last-value carried-
forward strategy as follows: in case if both pre–dose FEV1 values was missing at Visit 6/ET, the last value observed under treatment before Visit 6/ET was imputed as Visit 6/ET value. If there is no such last value under treatment, no imputation was made. If there is only one assessment of FEV1 pre-dose values at Visit 0 or Visit 6/ET is done, the available value was used for analysis.

End point type	Primary

End point timeframe:

End of 12 weeks treatment period

End point values	Salmeterol/Fluticasone DPI HEXAL (6-11 years) - PPS	Seretide 100 Accuhaler (6-11 years) - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96	98		
Units: Litre				
arithmetic mean (standard deviation)				
Baseline, FEV1	1.377 (± 0.296)	1.402 (± 0.275)		
Endpoint, FEV1	1.853 (± 0.439)	1.865 (± 0.4)		
Relative Change from Baseline (%)	35.4 (± 21.37)	33.9 (± 19.97)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

An Analysis of Covariance (ANCOVA) using treatment and centre as factors and baseline FEV1 (mean of the 2 pre-dose values at Visit 0) and age as co-variables was performed on the change.

Comparison groups	Salmeterol/Fluticasone DPI HEXAL (6-11 years) - PPS v Seretide 100 Accuhaler (6-11 years) - PPS
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.646
Method	ANCOVA
Parameter estimate	Mean Difference
Point estimate	0.011932

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.039171
upper limit	0.063036

Primary: The area under the 4-hour serial FEV1 curve (AUC0-4) at the end of the 12-week treatment period (Visit 6) relative to the mean FEV1 value at Visit 6 pre-inhalation

End point title	The area under the 4-hour serial FEV1 curve (AUC0-4) at the end of the 12-week treatment period (Visit 6) relative to the mean FEV1 value at Visit 6 pre-inhalation

End point description:

The area under the 4-hour serial FEV1 curve
(AUC0-4) at the end of the 12-week treatment period (Visit 6) relative to the mean FEV1 value at Visit 6 pre-inhalation. Missing values of the second primary endpoint 'FEV1 AUC(0-4)' were replaced using linear interpolation.

End point type	Primary

End point timeframe:

At the end of the double blind treatment period

End point values	Salmeterol/Fluticasone DPI HEXAL (6-11 years) - PPS	Seretide 100 Accuhaler (6-11 years) - PPS		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	96	98		
Units: Litre				
arithmetic mean (standard deviation)				
FEV1 pre-IP Inhalation	1.853 (± 0.439)	1.865 (± 0.4)		
AUC(0—4)/4 (L) at V6/ET	1.92 (± 0.45)	1.959 (± 0.423)		
Ratio of AUC(0—4)/4 and FEV1 pre-IP Inhalation	1.039 (± 0.059)	1.052 (± 0.081)		

Statistical analyses

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

An Analysis of Covariance (ANCOVA) was performed using treatment and centre as factors, age and log transformed pre-inhalation FEV1 as co-variables.

Comparison groups	Salmeterol/Fluticasone DPI HEXAL (6-11 years) - PPS v Seretide 100 Accuhaler (6-11 years) - PPS

Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.142
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	0.987814
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.971726
upper limit	1.004169

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first intake of investigational product (IP) till the patient's last study visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Salmeterol/Fluticasone DPI HEXAL (4-5 years) - Safety Set
Reporting group description: -	
Reporting group title	Seretide 100 Accuhaler (4-5 years) - Safety Set
Reporting group description: -	
Reporting group title	Seretide 100 Accuhaler (6-11 years) - Safety Set
Reporting group description: -	
Reporting group title	Salmeterol/Fluticasone DPI HEXAL (6-11 years) - Safety Set

Reporting group description: -

Serious adverse events	Salmeterol/Fluticasone DPI HEXAL (4-5 years) - Safety Set	Seretide 100 Accuhaler (4-5 years) - Safety Set	Seretide 100 Accuhaler (6-11 years) - Safety Set
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	2 / 102 (1.96%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory tract infection viral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Salmeterol/Fluticasone DPI HEXAL (6-11 years) - Safety Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection viral			
subjects affected / exposed	0 / 100 (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: 0 %

Non-serious adverse events	Salmeterol/Fluticasone DPI HEXAL (4-5 years) - Safety Set	Seretide 100 Accuhaler (4-5 years) - Safety Set	Seretide 100 Accuhaler (6-11 years) - Safety Set
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 10 (40.00%)	4 / 6 (66.67%)	39 / 102 (38.24%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Traumatic arthritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 6 (16.67%)	1 / 102 (0.98%)
occurrences (all)	0	1	3
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 6 (16.67%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 6 (16.67%)	1 / 102 (0.98%)
occurrences (all)	1	1	1
Gastritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorder			

subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Nasal septum deviation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 10 (0.00%)	1 / 6 (16.67%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Growth retardation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Jaw cyst			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0

Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Bronchopneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Ear lobe infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Herpes dermatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	3 / 102 (2.94%)
occurrences (all)	0	0	3
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 6 (0.00%)	3 / 102 (2.94%)
occurrences (all)	1	0	4
Laryngitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 6 (16.67%)	9 / 102 (8.82%)
occurrences (all)	0	1	9
Respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	4 / 102 (3.92%)
occurrences (all)	0	0	5
Respiratory tract infection viral			
subjects affected / exposed	1 / 10 (10.00%)	1 / 6 (16.67%)	9 / 102 (8.82%)
occurrences (all)	1	1	9
Rhinitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	4 / 102 (3.92%)
occurrences (all)	0	0	4
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0

Skin infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 102 (0.98%)
occurrences (all)	0	0	1
Tracheitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	1 / 6 (16.67%)	3 / 102 (2.94%)
occurrences (all)	1	1	3
Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Varicella			
subjects affected / exposed	0 / 10 (0.00%)	1 / 6 (16.67%)	0 / 102 (0.00%)
occurrences (all)	0	1	0
Viral rhinitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	2 / 102 (1.96%)
occurrences (all)	0	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	4 / 102 (3.92%)
occurrences (all)	0	0	5

Non-serious adverse events	Salmeterol/Fluticasone DPI HEXAL (6-11 years) - Safety Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 100 (48.00%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Traumatic arthritis			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences (all)	0		

Nervous system disorders			
Headache			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 100 (3.00%)		
occurrences (all)	4		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences (all)	4		
Gastritis			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorder			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 100 (3.00%)		
occurrences (all)	3		
Cough			

subjects affected / exposed	2 / 100 (2.00%)		
occurrences (all)	2		
Nasal septum deviation			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Dysphonia			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Growth retardation			
subjects affected / exposed	3 / 100 (3.00%)		
occurrences (all)	3		
Jaw cyst			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences (all)	2		
Bronchopneumonia			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences (all)	0		
Ear lobe infection			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Herpes dermatitis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Influenza			

subjects affected / exposed	3 / 100 (3.00%)			
occurrences (all)	3			
Nasopharyngitis				
subjects affected / exposed	7 / 100 (7.00%)			
occurrences (all)	7			
Laryngitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	5 / 100 (5.00%)			
occurrences (all)	5			
Respiratory tract infection				
subjects affected / exposed	8 / 100 (8.00%)			
occurrences (all)	11			
Respiratory tract infection viral				
subjects affected / exposed	6 / 100 (6.00%)			
occurrences (all)	6			
Rhinitis				
subjects affected / exposed	5 / 100 (5.00%)			
occurrences (all)	6			
Sinusitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences (all)	1			
Skin infection				
subjects affected / exposed	0 / 100 (0.00%)			
occurrences (all)	0			
Tracheitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences (all)	1			
Upper respiratory tract infection				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences (all)	3			
Urinary tract infection				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences (all)	2			
Varicella				

subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Viral rhinitis			
subjects affected / exposed	3 / 100 (3.00%)		
occurrences (all)	4		
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported