Clinical trial results:
Efficacy and safety of Salmeterol/Fluticasone DPI HEXAL versus SeretideTM AccuhalerTM in adolescent and adult patients with moderate-to-severe persistent asthma: A 12-week, multicenter, randomized, double-blind, double-dummy, parallel group study

Summary

EudraCT number	2007-005620-32
Trial protocol	HU 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 Ariticel 46 was wrong

Trial information

Trial identification

Sponsor protocol code	2006-56-DPI-1

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	10 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 AccuhalerTM in adolescent and adult patients suffering from moderate-to-severe persistent 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	14 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	Hungary: 42
Country: Number of subjects enrolled	Lithuania: 37
Country: Number of subjects enrolled	Poland: 156
Country: Number of subjects enrolled	Romania: 127
Country: Number of subjects enrolled	Ukraine: 193
Worldwide total number of subjects	555
EEA total number of subjects	362

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)	0
Adolescents (12-17 years)	48
Adults (18-64 years)	506
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A 12-week, multicenter, randomized, double-blind, double-dummy, parallel group study in adolescent and adult patients with moderate-to-severe persistent asthma

Pre-assignment

Screening details:

A total number of 592 patients where screened and 555 patients were randomized. The study consisted of a 2-week run-in period and a 12-week blinded treatment period (14 weeks in total). The screening visit (Visit -1) was followed by a 2-week run-in period during which all asthma treatments except reliever medication were to be stopped.

Pre-assignment period milestones

Number of subjects started	592[1]
Number of subjects completed	555

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Adverse event, non-fatal: 2
Reason: Number of subjects	Adverse event, serious non-fatal: 1
Reason: Number of subjects	Consent withdrawn by subject: 6
Reason: Number of subjects	Pregnancy: 2
Reason: Number of subjects	Protocol deviation: 1
Reason: Number of subjects	Lost to follow-up: 1
Reason: Number of subjects	Ineligibility: 23
Reason: Number of subjects	Other: 1

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: 37 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 (50 µg/100 µg)

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

Arm title	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg)
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/500 µg fluticasone per actuation), one actuation two times per day

Arm title	Seretide 500 Accuhaler
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Seretide 500 Accuhaler
Investigational medicinal product code	
Other name	NA
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

Seretide 500 Accuhaler (50 µg salmeterol/500 µg fluticasone per actuation), one actuation two times per day

Number of subjects in period 1	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg)	Seretide 100 Accuhaler	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg)
Started	139	137	136
Completed	136	131	128
Not completed	3	6	8
Consent withdrawn by subject	1	1	3
The blind was broken	-	-	2
Adverse event, non-fatal	1	1	1
Lost to follow-up	1	4	-
Protocol deviation	-	-	2

Number of subjects in period 1	Seretide 500 Accuhaler

Started	143
Completed	138
Not completed	5
Consent withdrawn by subject	2
The blind was broken	-
Adverse event, non-fatal	1
Lost to follow-up	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg)
Reporting group description: -	
Reporting group title	Seretide 100 Accuhaler
Reporting group description: -	
Reporting group title	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg)
Reporting group description: -	
Reporting group title	Seretide 500 Accuhaler
Reporting group description: -	

Reporting group values	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg)	Seretide 100 Accuhaler	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg)
Number of subjects	139	137	136
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)	0	0	0
Adolescents (12-17 year)	10	12	14
From 18 - 64 years	129	125	122
From 65 – 84 years	0	0	0
Over 85 years	0	0	0
Age Continuous			
Age Continuous Characteristic			
Units: Years			
arithmetic mean	45.9	45.5	43.8
standard deviation	± 14.9	± 14.4	± 14.9
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	92	77	83
Male	47	60	53

Reporting group values	Seretide 500 Accuhaler	Total	
Number of subjects	143	555	
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0	0	
Preterm newborn- gestational age < 37 wk	0	0	
Newborns (0-27days)	0	0	

Infants and toddlers (28days – 23months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 year)	12	48	
From 18 - 64 years	130	506	
From 65 – 84 years	1	1	
Over 85 years	0	0	
Age Continuous			
Age Continuous Characteristic			
Units: Years			
arithmetic mean	45.6		
standard deviation	± 14.2	-	
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	76	328	
Male	67	227	

End points

End points reporting groups

Reporting group title	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg)
Reporting group description: -	
Reporting group title	Seretide 100 Accuhaler
Reporting group description: -	
Reporting group title	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg)
Reporting group description: -	
Reporting group title	Seretide 500 Accuhaler
Reporting group description: -	
Subject analysis set title	Seretide 100 Accuhaler - 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 one IP.	
Subject analysis set title	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg) - 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 one IP.	
Subject analysis set title	Seretide 500 Accuhaler - 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 one IP.	
Subject analysis set title	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg) - 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 one IP.	
Subject analysis set title	Seretide 500 Accuhaler - 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 (50 µg/500 µg) - 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 (50 µg/100 µg) - 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	Seretide 100 Accuhaler - 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	Seretide 100 Accuhaler - 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 500 Accuhaler - 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	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg) - 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	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg) - 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: Change in FEV1 from baseline to the end of treatment period

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

End point description:

The absolute change in FEV1 from baseline at the end of
the 12-week treatment period. Missing values of the primary endpoint 'absolute 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	Seretide 100 Accuhaler - PPS	Seretide 500 Accuhaler - PPS	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg) - PPS	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg) - PPS
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	129	134	127	134
Units: Litre				
arithmetic mean (standard deviation)				
Baseline, FEV1	2.097 (± 0.537)	2.177 (± 0.538)	2.063 (± 0.509)	1.986 (± 0.514)
Endpoint, FEV1	2.464 (± 0.776)	2.561 (± 0.812)	2.406 (± 0.696)	2.262 (± 0.699)
Absolute Change from Baseline	0.367 (± 0.423)	0.384 (± 0.451)	0.344 (± 0.385)	0.276 (± 0.42)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis of covariance (ANCOVA) was applied including treatment group and center as factors, age and

baseline FEV1 as covariables in the statistical model in order to calculate a two-sided 95% confidence interval (CI) for the difference in treatment effects (based on the adjusted means).

Comparison groups	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg) - PPS v Seretide 100 Accuhaler - PPS
Number of subjects included in analysis	263
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.149
Method	ANCOVA
Parameter estimate	Mean Difference
Point estimate	-0.065446
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.154491
upper limit	0.0236

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis of covariance (ANCOVA) was applied including treatment group and center as factors, age and baseline FEV1 as covariables in the statistical model in order to calculate a two-sided 95% confidence interval (CI) for the difference in treatment effects (based on the adjusted means).

Comparison groups	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg) - PPS v Seretide 500 Accuhaler - PPS
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.482
Method	ANCOVA
Parameter estimate	Mean Difference
Point estimate	-0.032006
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.121478
upper limit	0.057465

Primary: Area Under the 12-hour Serial FEV1 Curve (AUC0-12) Relative to the Mean Pre-inhalation FEV1 at Visit 6

End point title	Area Under the 12-hour Serial FEV1 Curve (AUC0-12) Relative to the Mean Pre-inhalation FEV1 at Visit 6

End point description:

The area under the 12-hour serial FEV1 curve
(AUC0-12) 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(0-12)’ were replaced using linear interpolation.

End point type	Primary

End point timeframe:

At the end of the double blind treatment period

End point values	Seretide 100 Accuhaler - PPS	Seretide 500 Accuhaler - PPS	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg) - PPS	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg) - PPS
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	129	134	127	134
Units: Litre				
arithmetic mean (standard deviation)				
FEV1 mean of the 2 pre-dose values at Visit 6/ET	2.464 (± 0.776)	2.561 (± 0.812)	2.406 (± 0.696)	2.262 (± 0.699)
FEV1 AUC0-12/12	2.561 (± 0.774)	2.654 (± 0.802)	2.539 (± 0.715)	2.369 (± 0.699)
Ratio of FEV1 AUC0-12/12 & pre-IP FEV1	1.046 (± 0.075)	1.043 (± 0.082)	1.055 (± 0.078)	1.054 (± 0.09)
Log of the ratio of FEV1 AUC0-12/12 & pre-IP FEV1	0.043 (± 0.069)	0.039 (± 0.073)	0.051 (± 0.072)	0.05 (± 0.082)

Statistical analyses

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Analysis of covariance (ANCOVA)was applied including treatment group and center as factors, age and log transformed mean FEV1 pre-inhalation value as covariates in the statistical model in order to calculate a two-sided 95% confidence interval for the difference in treatment effects (based on the adjusted means).

Comparison groups	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg) - PPS v Seretide 100 Accuhaler - PPS
Number of subjects included in analysis	263
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.902
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	1.001062
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.984215
upper limit	1.018198

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Analysis of covariance (ANCOVA)was applied including treatment group and center as factors, age and log transformed mean FEV1 pre-inhalation value as covariates in the statistical model in order to calculate a two-sided 95% confidence interval for the difference in treatment effects (based on the adjusted means).

Comparison groups	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg) - PPS v Seretide 500 Accuhaler - PPS
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.333
Method	ANCOVA
Parameter estimate	Ratio
Point estimate	1.008245
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.991557
upper limit	1.025214

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first intake of investigational product (IP) till the 4 weeks after the last intake of IP

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg) - Safety Set
Reporting group description: -	
Reporting group title	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg) - Safety Set
Reporting group description: -	
Reporting group title	Seretide 500 Accuhaler - Safety Set
Reporting group description: -	
Reporting group title	Seretide 100 Accuhaler - Safety Set

Reporting group description: -

Serious adverse events	Salmeterol/Fluticasone DPI HEXAL (50 µg/100 µg) - Safety Set	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg) - Safety Set	Seretide 500 Accuhaler - Safety Set
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 139 (0.00%)	1 / 136 (0.74%)	0 / 143 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 139 (0.00%)	1 / 136 (0.74%)	0 / 143 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Seretide 100 Accuhaler - Safety Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 137 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Loss of consciousness			

subjects affected / exposed	0 / 137 (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 (50 µg/100 µg) - Safety Set	Salmeterol/Fluticasone DPI HEXAL (50 µg/500 µg) - Safety Set	Seretide 500 Accuhaler - Safety Set
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 139 (27.34%)	33 / 136 (24.26%)	35 / 143 (24.48%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 139 (0.00%)	1 / 136 (0.74%)	0 / 143 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	1	0	0
Extrasystoles			
subjects affected / exposed	0 / 139 (0.00%)	1 / 136 (0.74%)	0 / 143 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	1 / 143 (0.70%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	1 / 143 (0.70%)
occurrences (all)	0	0	1
Tachycardia			

subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	1	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	1 / 143 (0.70%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	5 / 139 (3.60%)	0 / 136 (0.00%)	4 / 143 (2.80%)
occurrences (all)	5	0	4
Tremor			
subjects affected / exposed	2 / 139 (1.44%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 139 (0.00%)	1 / 136 (0.74%)	0 / 143 (0.00%)
occurrences (all)	0	1	0
Lymphadenitis			
subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	2 / 139 (1.44%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			
subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	1

Nausea			
subjects affected / exposed	1 / 139 (0.72%)	2 / 136 (1.47%)	1 / 143 (0.70%)
occurrences (all)	1	2	1
Toothache			
subjects affected / exposed	2 / 139 (1.44%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	2	0	0
Vomiting			
subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 139 (2.16%)	3 / 136 (2.21%)	2 / 143 (1.40%)
occurrences (all)	3	3	2
Dysphonia			
subjects affected / exposed	3 / 139 (2.16%)	6 / 136 (4.41%)	2 / 143 (1.40%)
occurrences (all)	3	6	2
Nasal congestion			
subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 139 (0.72%)	1 / 136 (0.74%)	0 / 143 (0.00%)
occurrences (all)	1	1	0
Throat irritation			
subjects affected / exposed	2 / 139 (1.44%)	1 / 136 (0.74%)	1 / 143 (0.70%)
occurrences (all)	2	2	1
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	1
Infections and infestations			
Acute tonsillitis			

subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 139 (0.72%)	2 / 136 (1.47%)	1 / 143 (0.70%)
occurrences (all)	1	2	1
Candidiasis			
subjects affected / exposed	0 / 139 (0.00%)	1 / 136 (0.74%)	0 / 143 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 139 (0.00%)	2 / 136 (1.47%)	4 / 143 (2.80%)
occurrences (all)	0	2	4
Erysipelas			
subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	6 / 139 (4.32%)	5 / 136 (3.68%)	4 / 143 (2.80%)
occurrences (all)	6	5	4
Oral candidiasis			
subjects affected / exposed	0 / 139 (0.00%)	1 / 136 (0.74%)	2 / 143 (1.40%)
occurrences (all)	0	1	2
Respiratory tract infection			
subjects affected / exposed	1 / 139 (0.72%)	1 / 136 (0.74%)	2 / 143 (1.40%)
occurrences (all)	1	1	2
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	1
Respiratory tract infection viral			
subjects affected / exposed	4 / 139 (2.88%)	1 / 136 (0.74%)	4 / 143 (2.80%)
occurrences (all)	4	1	5
Rhinitis			
subjects affected / exposed	1 / 139 (0.72%)	3 / 136 (2.21%)	0 / 143 (0.00%)
occurrences (all)	1	3	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 139 (0.72%)	3 / 136 (2.21%)	6 / 143 (4.20%)
occurrences (all)	2	3	7
Sinusitis			

subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	1 / 143 (0.70%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	2 / 139 (1.44%)	1 / 136 (0.74%)	0 / 143 (0.00%)
occurrences (all)	2	1	0
Viral pharyngitis			
subjects affected / exposed	0 / 139 (0.00%)	1 / 136 (0.74%)	0 / 143 (0.00%)
occurrences (all)	0	1	0
Viral rhinitis			
subjects affected / exposed	1 / 139 (0.72%)	0 / 136 (0.00%)	1 / 143 (0.70%)
occurrences (all)	1	0	1
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 139 (0.00%)	0 / 136 (0.00%)	0 / 143 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 139 (0.00%)	1 / 136 (0.74%)	0 / 143 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Seretide 100 Accuhaler - Safety Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 137 (22.63%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Angina pectoris			

subjects affected / exposed occurrences (all) Extrasystoles subjects affected / exposed occurrences (all) Palpitations subjects affected / exposed occurrences (all) Sinus tachycardia subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all) Ventricular extrasystoles subjects affected / exposed occurrences (all)	0 / 137 (0.00%) 0 0 / 137 (0.00%) 0 0 / 137 (0.00%) 0 0 / 137 (0.00%) 0 1 / 137 (0.73%) 1 1 / 137 (0.73%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all)	 0 / 137 (0.00%) 0 1 / 137 (0.73%) 1 0 / 137 (0.00%) 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymphadenitis subjects affected / exposed occurrences (all)	 0 / 137 (0.00%) 0 1 / 137 (0.73%) 1		
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences (all)	2		
Toothache			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Dysphonia			
subjects affected / exposed	4 / 137 (2.92%)		
occurrences (all)	4		
Nasal congestion			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Throat irritation			

subjects affected / exposed occurrences (all)	3 / 137 (2.19%) 3		
Skin and subcutaneous tissue disorders Psoriasis subjects affected / exposed occurrences (all)	 1 / 137 (0.73%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 0 / 137 (0.00%) 0		
Infections and infestations Acute tonsillitis subjects affected / exposed occurrences (all)	 1 / 137 (0.73%) 1		
Bronchitis subjects affected / exposed occurrences (all)	 2 / 137 (1.46%) 2		
Candidiasis subjects affected / exposed occurrences (all)	 0 / 137 (0.00%) 0		
Influenza subjects affected / exposed occurrences (all)	 4 / 137 (2.92%) 4		
Erysipelas subjects affected / exposed occurrences (all)	 0 / 137 (0.00%) 0		
Nasopharyngitis subjects affected / exposed occurrences (all)	 6 / 137 (4.38%) 6		
Oral candidiasis subjects affected / exposed occurrences (all)	 1 / 137 (0.73%) 1		
Respiratory tract infection subjects affected / exposed occurrences (all)	 2 / 137 (1.46%) 2		
Oropharyngeal candidiasis			

subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Respiratory tract infection viral			
subjects affected / exposed	3 / 137 (2.19%)		
occurrences (all)	3		
Rhinitis			
subjects affected / exposed	2 / 137 (1.46%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Viral infection			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		
Viral pharyngitis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Viral rhinitis			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 137 (0.73%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 137 (0.00%)		
occurrences (all)	0		

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