Clinical trial results:
A 12-Week, Double-Blind, Randomised, Multi-Centre, Parallel-Group Study Evaluating the Efficacy, Safety, and Patient Use (User Study) of Symbicort®1 (Budesonide/Formoterol) Breath-Actuated Metered Dose Inhaler (BA MDI) 2x160/4.5 g Twice Daily Compared with Symbicort® (Budesonide/Formoterol) AC (Actuation Counter) pMDI 2x160/4.5 g Twice Daily and Budesonide AC pMDI 2x160 g Twice Daily in Adult and Adolescent Asthmatics

Summary

EudraCT number	2011-002523-17
Trial protocol	HU BG
Global end of trial date	02 March 2013

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	D589OC00003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	AstraZeneca R&D, SE-431 83 Mölndal, Sweden,
Public contact	Dr Ulf Nihlen, MD, AstraZeneca, aztrial_results_posting@astrazeneca.com
Scientific contact	Dr Ulf Nihlen, MD, AstraZeneca, aztrial_results_posting@astrazeneca.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	02 March 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 March 2013
Global end of trial reached?	Yes
Global end of trial date	02 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of Symbicort BA MDI 2x160/4.5 µg bid with that of Symbicort AC pMDI 2x160/4.5 µg bid by evaluation of: forced expiratory volume during first second (FEV1), 60 minutes post-dose and FEV1 pre-dose.

Protection of trial subjects:

The Institutional review board (IRB)/independent ethics committee (IEC) for each study site approved the final clinical study protocol (CSP), including the final version of the informed consent form (ICF) and any other written information and/or materials that were provided to the patients.

The PI at each centre ensured that each patient was given full and adequate oral and written information about the nature, purpose, possible risk, and benefit of the study. Each patient was notified that they were free to discontinue from the study at any time. Patients were given the opportunity to ask questions and were allowed time to consider the information provided.

The PI at each centre ensured that each patient provided signed and dated informed consent before conducting any procedure specifically for the study. In patients below the age of consent, informed consent was obtained from both the patient and the patient’s parent/legal guardian

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 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	Hungary: 38
Country: Number of subjects enrolled	United States: 150
Country: Number of subjects enrolled	Bulgaria: 26
Worldwide total number of subjects	214
EEA total number of subjects	64

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)	21
Adults (18-64 years)	178
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicentre trial conducted in 3 countries between November 2011 and August 2012.

Pre-assignment

Screening details:

The study consisted from an enrolment visit, a 2- week run in (standardization) period, randomization at visit 4, and 3 further visits (visits 5- 7) at 3, 7 and 12 weeks. During the 2-week-run-in period patients were treated with budesonide AC pMDI 2x160µg bid. After this period subjects were randomized to receive 1 of 3 doouble blinded treatments.

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, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Symbicort BA MDI

Arm description:

Symbicort BA MDI 2x160/4.5 µg twice daily

Arm type	Experimental
Investigational medicinal product name	Symbicort BA MDI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Symbicort BA MDI 2x160/4.5 µg twice daily

Arm title	Symbicort pMDI

Arm description:

Symbicort AC pDMI 2x160/4.5 µg twice daily

Arm type	Experimental
Investigational medicinal product name	Symbicort pMDI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Symbicort pMDI 2x160/4.5 µg twice daily

Arm title	Budesonide

Arm description:

Budesonide AC pMDI 2x160 µg twice daily

Arm type	Active comparator

Investigational medicinal product name	Budesonide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Budesonide pMDI 2x160 µg twice daily

Number of subjects in period 1	Symbicort BA MDI	Symbicort pMDI	Budesonide
Started	71	71	72
Completed	63	67	65
Not completed	8	4	7
Consent withdrawn by subject	4	-	2
Adverse event, non-fatal	2	3	3
Eligibility criteria + other	2	1	1
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Symbicort BA MDI
Reporting group description:	
Symbicort BA MDI 2x160/4.5 µg twice daily	
Reporting group title	Symbicort pMDI
Reporting group description:	
Symbicort AC pDMI 2x160/4.5 µg twice daily	
Reporting group title	Budesonide
Reporting group description:	
Budesonide AC pMDI 2x160 µg twice daily	

Reporting group values	Symbicort BA MDI	Symbicort pMDI	Budesonide
Number of subjects	71	71	72
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	6	8	7
Adults (18-64 years)	60	56	62
From 65-84 years	5	7	3
85 years and over	0	0	0
Age Continuous | Units: Years			
arithmetic mean	42.83	42.62	42.72
standard deviation	± 16.156	± 16.873	± 14.424
Gender, Male/Female Units: Participants			
Female	37	47	35
Male	34	24	37
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	4	1	1
Native Hawaiian or Other Pacific Islander	0	0	1
Black or African American	9	7	11
White	57	63	57
More than one race	0	0	0
Unknown or Not Reported	1	0	2
Years since asthma diagnosis Units: years			
arithmetic mean	24.26	24.12	24.38
standard deviation	± 14.891	± 15.128	± 15.183

Reporting group values	Total		
Number of subjects	214		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	21		
Adults (18-64 years)	178		
From 65-84 years	15		
85 years and over	0		
Age Continuous | Units: Years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: Participants			
Female	119		
Male	95		
Race Units: Subjects			
American Indian or Alaska Native	0		
Asian	6		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	27		
White	177		
More than one race	0		
Unknown or Not Reported	3		
Years since asthma diagnosis Units: years			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups	
Reporting group title	Symbicort BA MDI
Reporting group description:	
Symbicort BA MDI 2x160/4.5 µg twice daily	
Reporting group title	Symbicort pMDI
Reporting group description:	
Symbicort AC pDMI 2x160/4.5 µg twice daily	
Reporting group title	Budesonide
Reporting group description:	
Budesonide AC pMDI 2x160 µg twice daily	

Primary: Forced expiratory volume in 1 second (FEV1) - Post dose	
End point title	Forced expiratory volume in 1 second (FEV1) - Post dose
End point description:	
Descriptive statistics for post-dose FEV1 (L) by visit; Baseline defined as the last pre-dose value prior to 1st dose of randomized therapy. Trt Avg = Mean of all available valid values after randomization.	
End point type	Primary
End point timeframe:	
60 minutes post-dose in clinic visits at baseline, and week 3, 7, 12	

End point values	Symbicort BA MDI	Symbicort pMDI	Budesonide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	71	71	
Units: Liter				
geometric mean (geometric coefficient of variation)				
Baseline (Week 0)	2.09 (± 31.46)	1.97 (± 27.16)	2.12 (± 26.34)	
Week 0	2.49 (± 32.14)	2.35 (± 25.97)	2.28 (± 27.18)	
Week 3	2.52 (± 31.98)	2.34 (± 26.31)	2.3 (± 30.22)	
Week 7	2.59 (± 32.17)	2.35 (± 27.22)	2.33 (± 29.29)	
Week 12	2.52 (± 30.71)	2.39 (± 27.31)	2.3 (± 28.27)	
Treatment Average	2.53 (± 30.57)	2.37 (± 26.33)	2.3 (± 28.36)	

Statistical analyses

Statistical analysis title	FEV1 - Symbicort pMDI vs Budesonide
Statistical analysis description:	
The comparison of Symbicort AC pMDI 2x160/4.5 µg bid with budesonide AC pMDI 2x160 µg bid for post dose FEV1	
Comparison groups	Symbicort pMDI v Budesonide

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Estimated Geometic Mean Ratio
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.14

Statistical analysis title	FEV1 - Symbicort BA MDI vs Symbicort pMDI

Statistical analysis description:

The comparisons of Symbicort BA MDI 2x160/4.5 µg bid with Symbicort AC pMDI 2x160/4.5 µg bid for post dose FEV1.

Comparison groups	Symbicort BA MDI v Symbicort pMDI
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.547
Method	ANCOVA
Parameter estimate	Estimated Geometric Mean Ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.05

Notes:

[1] - Assuming a standard deviation of 0.2 (for pre dose FEV1) on the log-scale and 60 patients/arm, the width of the confidence interval will extend 0.072 from the point estimate on the log-scale. The lower and upper limits of the CI for the ratio of effects will thus be obtained by multiplying the estimated ratio by 0.931 and 1.075, respectively.

Primary: Forced expiratory volume in 1 second (FEV1) - Pre dose

End point title	Forced expiratory volume in 1 second (FEV1) - Pre dose

End point description:

Descriptive statistics for predose FEV1(L) by visit; Baseline defined as the last pre-dose value prior to 1st dose of randomized therapy. Trt Avg = Mean of all available valid values after randomization.

End point type	Primary

End point timeframe:

Pre AM dose in clinic visits at baseline, and week 3, 7, 12

End point values	Symbicort BA MDI	Symbicort pMDI	Budesonide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	71	71	
Units: Liters				
geometric mean (geometric coefficient of variation)				
Baseline (Week 0)	2.09 (± 31.46)	1.97 (± 27.16)	2.12 (± 26.34)	
Week 3	2.32 (± 32.79)	2.12 (± 28.29)	2.22 (± 31.21)	
Week 7	2.4 (± 32.86)	2.11 (± 29.96)	2.25 (± 29.01)	
Week 12	2.34 (± 30.84)	2.17 (± 31.29)	2.23 (± 30.15)	
Average of treatment period	2.34 (± 30.15)	2.15 (± 29.15)	2.23 (± 29.36)	

Statistical analyses

Statistical analysis title	FEV1 pre-dose - Symbicort BA MDI vs Symbicort pMDI

Statistical analysis description:

The comparisons of Symbicort BA MDI 2x160/4.5 µg bid with Symbicort AC pMDI 2x160/4.5 µg bid, for pre-dose FEV1.

Comparison groups	Symbicort BA MDI v Symbicort pMDI
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.131
Method	ANCOVA
Parameter estimate	Estimated Geometric Mean Ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.08

Notes:

[2] - Assuming a standard deviation of 0.2 (for pre dose FEV1) on the log-scale and 60 patients/arm, the width of the confidence interval will extend 0.072 from the point estimate on the log-scale. The lower and upper limits of the CI for the ratio of effects will thus be obtained by multiplying the estimated ratio by 0.931 and 1.075, respectively.

Secondary: Peak expiratory flow

End point title	Peak expiratory flow

End point description:

End point type	Secondary

End point timeframe:

Recorded morning upon rising and evening before sleep for 14 weeks

End point values	Symbicort BA MDI	Symbicort pMDI	Budesonide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	71	71	
Units: L/Min				
arithmetic mean (standard deviation)				
Morning Peak expiratory flow (Baseline)	357.95 (± 100.59)	335.7 (± 102.99)	360.46 (± 103.09)	
Evening Peak expiratory flow (Baseline)	364.61 (± 103.62)	347.86 (± 110.8)	367.64 (± 102.73)	
Evening Peak expiratory flow (Treatment Average)	379.96 (± 104.72)	362.99 (± 112.63)	348.94 (± 97.94)	
Morning Peak expiratory flow (Treatment Average)	376.28 (± 106.76)	353.69 (± 108.72)	343.59 (± 98.12)	

Statistical analyses

Statistical analysis title	mPEF - Symbicort BA MDI vs Symbicort pMDI

Statistical analysis description:

Morning peak expiratory flow (mPEF): Comparing mean changes from baseline to the average of the double-blind treatment period between Symbicort BA MDI 2x160/4.5 µg bid and Symbicort AC pMDI 2x160/4.5 µg bid

Comparison groups	Symbicort BA MDI v Symbicort pMDI
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.825
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.81
upper limit	14.8
Variability estimate	Standard error of the mean
Dispersion value	6.75

Notes:

[3] - No adjustment were be made for multiplicity for these supportive variables and nominal p-values were reported.

Statistical analysis title	mPEF - Symbicort pMDI vs Budesonide

Statistical analysis description:

Morning peak expiratory flow (mPEF): Comparing mean changes from baseline to the average of the double-blind treatment period between Symbicort AC pMDI 2x160/4.5 µg bid minus Budesonide AC pMDI 2x160 µg bid

Comparison groups	Symbicort pMDI v Budesonide

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	33.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.11
upper limit	46.93
Variability estimate	Standard error of the mean
Dispersion value	6.8

Statistical analysis title	ePEF - Symbicort BA MDI vs Symbicort pMDI

Statistical analysis description:

Evening peak expiratory flow (ePEF): Comparing mean changes from baseline to the average of the double-blind treatment period between Symbicort BA MDI 2x160/4.5 µg bid and Symbicort AC pMDI 2x160/4.5 µg bid.

Comparison groups	Symbicort BA MDI v Symbicort pMDI
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.81
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.66
upper limit	13.61
Variability estimate	Standard error of the mean
Dispersion value	6.15

Notes:

[4] - No adjustment were made for multiplicity for these supportive variables and nominal p-values were reported.

Statistical analysis title	ePEF - Symbicort pMDi vs Budesonide

Statistical analysis description:

Evening peak expiratory flow (ePEF): Comparing mean changes from baseline to the average of the double-blind treatment period between Symbicort AC pMDI 2x160/4.5 µg bid and Budesonide AC pMDI 2x160 µg bid.

Comparison groups	Symbicort pMDI v Budesonide

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	32.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	20.01
upper limit	44.49
Variability estimate	Standard error of the mean
Dispersion value	6.21

Secondary: Asthma symptoms Score (Total)

End point title	Asthma symptoms Score (Total)

End point description:

The total score is calculated as sum of the morning and evening scores of each day and the treatment period mean score is defined as the mean of all total score recorded during the 12-week treatment period. Trt Avg=Mean total score of double-blind period values.(day/night score ranges from 0 to 3; 0=no asthma symptoms; 3= unable to do normal activities (or to sleep) due to asthma). Higher score represents worse outcome.

End point type	Secondary

End point timeframe:

Recorded between 6:00 – 11:00 AM from previous 12 hours and 6:00 -11:00 PM from previous 12 hours for 14 weeks

End point values	Symbicort BA MDI	Symbicort pMDI	Budesonide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	71	71	
Units: Asthma score on a scale of 0 to 3				
arithmetic mean (standard deviation)				
Baseline	2.04 (± 0.98)	1.92 (± 0.72)	2.12 (± 0.88)	
Treatment Average (Trt Avg)	1.68 (± 1.1)	1.45 (± 0.91)	2.02 (± 0.96)	

Statistical analyses

Statistical analysis title	Total Symptom score - Symb. BA MDI vs Symb. pMDI

Statistical analysis description:

Comparing mean changes from baseline to the average of the double-blind treatment period between Symbicort BA MDI 2x160/4.5 µg bid and Symbicort AC pMDI 2x160/4.5 µg bid.

Comparison groups	Symbicort BA MDI v Symbicort pMDI

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.272
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.35
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[5] - No adjustment were made for multiplicity for these supportive variables and nominal p-values were reported.

Secondary: Night-time awakenings due to asthma symptoms(% Awakening-free nights)

End point title	Night-time awakenings due to asthma symptoms(% Awakening-free nights)

End point description:

The percentage of days with no awakenings due to asthma. Baseline= Mean % awakening-free nights during run-in period ; Trt Avg=Mean % awakening-free nights during double-blind period.

End point type	Secondary

End point timeframe:

Recorded 6:00 – 11:00 AM for 14 weeks

End point values	Symbicort BA MDI	Symbicort pMDI	Budesonide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	71	71	
Units: Percentage of days with no awakenings				
arithmetic mean (standard deviation)				
Baseline	78.54 (± 28.97)	78.76 (± 29.76)	81.59 (± 25.32)	
Treatment Average (Trt Avg)	83.73 (± 30.9)	89.93 (± 21.4)	84.62 (± 26.31)	

Statistical analyses

Statistical analysis title	Nightime Awakenings - Symb. BA MDI vs Symb. pMDI

Statistical analysis description:

Comparing mean changes from baseline to the average of the double-blind treatment period between Symbicort BA MDI 2x160/4.5 µg bid and Symbicort AC pMDI 2x160/4.5 µg bid.

Comparison groups	Symbicort BA MDI v Symbicort pMDI

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.025
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.41
upper limit	-0.79
Variability estimate	Standard error of the mean
Dispersion value	2.69

Notes:

[6] - No adjustment were made for multiplicity for these supportive variables and nominal p-values were reported.

Secondary: Use of rescue medication day and night (Total daily rescue medication use)

End point title	Use of rescue medication day and night (Total daily rescue medication use)

End point description:

Total daily rescue medication use is calculated as the sum of morning and evening use each day and averaged over the 12 weeks treatment periods to calculate the treatment period mean. Baseline= Mean rescue medication used during run-in period ; Trt Avg=Mean rescue medication used during double-blind period.

End point type	Secondary

End point timeframe:

Recorded between 6:00 – 11:00 AM from previous 12 hours and 6:00 -11:00 PM from previous 12 hours for 14 weeks

End point values	Symbicort BA MDI	Symbicort pMDI	Budesonide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	71	71	
Units: Inhalations/24 hrs				
arithmetic mean (standard deviation)				
Baseline	2.55 (± 2.48)	2.19 (± 1.75)	2.65 (± 2.36)	
Treatment Average (Trt Avg)	1.81 (± 2.67)	1.26 (± 1.6)	2.34 (± 2.38)	

Statistical analyses

Statistical analysis title	Total Daily Rescue Med-Symb. BA MDI vs Symb. pMDI

Statistical analysis description:

Comparing mean changes from baseline to the average of the double-blind treatment period between BAI Symbicort BA MDI 2x160/4.5 µg bid and pMDI Symbicort AC pMDI 2x160/4.5 µg bid.

Comparison groups	Symbicort BA MDI v Symbicort pMDI

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.258
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.71
Variability estimate	Standard error of the mean
Dispersion value	0.23

Notes:

[7] - No adjustment were made for multiplicity for these supportive variables and nominal p-values were reported.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the enrolment visit (visit 1) until follow-up (14 weeks after randomisation). Events occurring on or after first dose of study medication are included in the summaries.

Adverse event reporting additional description:

1 patient from the Budesonide group has not taken any dose of the IP, so not included in the Safety population'.

A total of 19 patients reported non-serious adverse events; 19 on Budesonide, 21 on Symbicort BA MDI, 24 on Symbicort pMDI.. Numbers for non-serious AEs in the reporting group table are based on the 2% threshold frequency.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Budesonide

Reporting group description:

Budesonide AC pMDI 2x160 µg twice daily

Reporting group title	Symbicort BA MDI

Reporting group description:

Symbicort BA MDI 2x160/4.5 µg twice daily

Reporting group title	Symbicort pMDI

Reporting group description:

Symbicort AC pDMI 2x160/4.5 µg twice daily

Serious adverse events	Budesonide	Symbicort BA MDI	Symbicort pMDI
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 71 (1.41%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Budesonide	Symbicort BA MDI	Symbicort pMDI
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 71 (8.45%)	6 / 71 (8.45%)	9 / 71 (12.68%)
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 71 (4.23%)	1 / 71 (1.41%)	2 / 71 (2.82%)
occurrences (all)	3	1	2
Infections and infestations			
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	3 / 71 (4.23%)	2 / 71 (2.82%)	5 / 71 (7.04%)
occurrences (all)	3	2	5
UPPER RESPIRATORY TRACT INFECTION BACTERIAL			
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	0 / 71 (0.00%)
occurrences (all)	1	2	0
Bronchitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	3 / 71 (4.23%)
occurrences (all)	0	1	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 October 2011	Clarify the timing of spirometry measurements in the morning. To allow the patients to undergo rescreen, so that at rescreening the patients would meet the time requirements for various elements by Visit 2 in the inclusion criteria without changing the patient characterisation in the study or jeopardizing patient safety.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No. of participants in the safety analysis set is (71 for all the group) as 1 patients from the Budesonide group has not taken any dose of the IP, so not included in the Safety population.

Notes: