AstraZeneca

**Clinical Study Report Synopsis**

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|---|---|
| Drug Substance | Budesonide/formoterol |
| Study Code | D5890C00018 |
| Edition Number | 1 |
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# A Patient Follow-up Programme for patients using Symbicort® Turbuhaler® maintenance and reliever therapy in normal clinical practice

**Study dates:** First subject enrolled: 12 July 2007
Last subject last visit: 09 April 2010

**Phase of development:** Therapeutic use (IV)

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

## Study centre(s)

This report presents data from 5124 patients enrolled at 584 centres in 12 countries: Belgium, Bulgaria, Czech Republic, Denmark, Germany, Greece, Hungary, Netherlands, Norway, Portugal, Sweden and United Kingdom. Of the 5124 enrolled patients, 4622 patients had recorded diary data after inclusion in this programme. These 4622 were analysed in an Intention To Treat analysis. The first patient entered the study on July 12, 2007 and the last patient finished the study on April 9, 2010

## Publications

None at the time of writing this report.

## Objectives and criteria for evaluation

**Table S1 Objectives and outcome variables**

| **Outcome variables** | | | |
|---|---|---|---|
| **Priority** | **Description** | **Title and description** | **Method of assessment and derivation** |
| **Objective** | | **Outcome variables:** | |
| Primary | To investigate the extent of Symbicort Turbuhaler use in patients prescribed Symbicort Turbuhaler as maintenance and reliever therapy | **Primary outcome variable:**<br>The total daily use of Symbicort Turbuhaler | Total number of inhalations per day recorded by the patient in the IVRS on a daily basis. |
| | | **Other outcome variables:**<br>Number of as-needed inhalations of Symbicort Turbuhaler per day | Total number of as-needed inhalations per day recorded by the patient in the IVRS on a daily basis. |
| | | Number of maintenance inhalations of Symbicort Turbuhaler per day | Calculated difference between the total number of inhalations and the number of as-needed inhalations recorded by the patient in the IVRS on a daily basis. |

a) There are no safety variables. Adverse Drug reactions associated with Symbicort SMART were to be reported according to local requirements, as with any other markedet drug.

## Programme design

This is a 12-month, observational, non-comparative, Patient Follow-up Programme for asthma patients being prescribed Symbicort SMART in normal clinical practice before their inclusion in this programme.

**Target subject population and sample size**

The target population is asthma patients prescribed Symbicort SMART according to the approved EU label before being included in the Patient Follow-up Programme.

This is a descriptive programme without a control group and determination of the sample size is not based on any formal power calculation.

**Treatment**

Prior to being enrolled into this programme, the patients should have been prescribed Symbicort Turbuhaler according to the approved EU label for Symbicort SMART by the investigator and given treatment instructions according to normal clinical practice. For the analyses, the patients have been divided post-hoc into 3 treatment groups based on their prescribed daily maintenance dose of Symbicort Turbuhaler at inclusion : 160/9 µg, 320/9 µg, and 640/18 µg. Due to a protocol deviation, one patient was prescribed a Symbicort maintenance dose of 320/18 µg/daily (four inhalations of 80/4.5 µg). This patient is not reported separately but is included in the all patients group in the tables.

**Duration of treatment**

The patients have reported their use of Symbicort Turbuhaler during 12 months of treatment.

**Statistical methods**

The total daily use of Symbicort was extensively described. The focus was on patients with high daily Symbicort use, frequency of days with high Symbicort use, and patient's average daily Symbicort use during the programme. The analyses consists of descriptive statistics (number of observations, mean, standard deviation, minimum and maximum) and plots illustrating different aspects of the daily use of Symbicort.

In addition the daily number of as-needed inhalations and the daily number of maintenance inhalations was described separately using similar methods as for the total daily use.

Data has been presented both for all patients and separated by start dose (maintenance).

**Subject population**

A total of 5124 patients were enrolled at 584 centres in 12 countries

At one centre multiple severe deviations were discovered; including that data was entered into the IVR system by the clinic staff and not by patients, that clinic staff had been recruited in the study, and several irregularities in informed consent forms. Since the data from this site is regarded as not reliable, it is excluded from all analyses. This decision was formulated in a Letter of Assurance from the Symbicort Clinical project Team in August 2009. The 41 patients allegedly included at this site do not appear in any of the tables in this report, thus the number of enrolled patients is 5083 in all analyses.

The Full Analysis Set included all patients with diary data after inclusion in this follow-up programme. Of the 5083 enrolled patients, 4581 patients had recorded diary data after inclusion in this programme. These 4581 were included in the FAS. The first patient entered the programme on July 12, 2007 and the last patient finished the programme on April 9, 2010.

**Table S2 Patient flow**

| | 160/9 µg | 320/9 µg | 640/18 µg | All |
|---|---|---|---|---|
| **Enrolled patients** | | | | **5083** |
| Not included (no diary data) | | | | **502** |
| -No reason recorded | | | | **225** |
| -Incorrect enrolment | | | | **29** |
| -Terminated study treatment | | | | **7** |
| -Voluntary discontinuation by subject | | | | **138** |
| -Lost to follow-up | | | | **34** |
| -Severe non-compliance to protocol | | | | **69** |
| **Included** | **119** | **3106** | **1355** | **4581**[a] |
| **Not treated or no data on treatment** | **0** | **6** | **1** | **7** |
| **Discontinued** | **25** | **558** | **235** | **818** |
| -Incorrect enrolment | 3 | 21 | 10 | **34** |
| -Terminated study treatment | 1 | 59 | 46 | **106** |
| -Voluntary discontinuation by subject | 13 | 326 | 114 | **453** |
| -Lost to follow-up | 1 | 101 | 32 | **134** |
| -Severe non-compliance to protocol | 7 | 51 | 33 | **91** |
| **Completed** | **94** | **2542** | **1119** | **3756**[a] |

[a] including one patient wrongly prescribed 320/18ug

The treatment groups based on maintenance doses of Symbicort SMART at enrolment were balanced in terms of demographic and baseline characteristics.

**Summary of efficacy results**

In Table S3 summary statistics for mean use of Symbicort SMART is presented and Table S4 presents the percentage of days with different level of as-needed inhalations/day.

**Table S3 Summary statistics for mean use of Symbicort SMART**

| Variable | Group | n | Mean | Min | P01 | P05 | P10 | Median |
|---|---|---|---|---|---|---|---|---|
| **Number of inhalations in total/day** | 160/9 µg | 119 | 2.483 | 0.79 | 1.00 | 1.24 | 1.66 | 2.11 |
| | 320/9 µg | 3106 | 2.525 | 0.00 | 0.66 | 1.17 | 1.73 | 2.14 |
| | 640/18 µg | 1355 | 4.265 | 0.00 | 1.33 | 2.07 | 2.63 | 4.05 |
| | **All** | **4581**[a] | **3.039** | **0.00** | **0.82** | **1.36** | **1.88** | **2.44** |
| **Number of inhalations of maintenance medication/day** | 160/9 µg | 119 | 1.805 | 0.00 | 0.00 | 0.03 | 0.22 | 1.98 |
| | 320/9 µg | 3106 | 1.796 | 0.00 | 0.00 | 0.03 | 0.29 | 1.98 |
| | 640/18 µg | 1355 | 3.189 | 0.00 | 0.00 | 0.06 | 0.51 | 3.88 |
| | **All** | **4581**[a] | **2.209** | **0.00** | **0.00** | **0.03** | **0.33** | **2.00** |
| **Number of inhalations of as-needed medication/day** | 160/9 µg | 119 | 0.679 | 0.00 | 0.00 | 0.00 | 0.00 | 0.17 |
| | 320/9 µg | 3106 | 0.729 | 0.00 | 0.00 | 0.00 | 0.00 | 0.26 |
| | 640/18 µg | 1355 | 1.076 | 0.00 | 0.00 | 0.00 | 0.00 | 0.45 |
| | **All** | **4581**[a] | **0.831** | **0.00** | **0.00** | **0.00** | **0.00** | **0.30** |

[a] including one patient wrongly prescribed 320/18ug

**Table S4 Percentage of days with different level of as-needed inhalations/day (all patients, n=4622).**

| As-needed inhalations (x) | All patients exactly x/day | at most x/day | at least x/day |
|---|---|---|---|
| 0 | 62.75 | 62.75 | 100.00 |
| 1 | 11.62 | 74.37 | 37.25 |
| 2 | 16.56 | 90.93 | 25.63 |
| 3 | 2.58 | 93.51 | 9.07 |

| As-needed inhalations (x) | All patients exactly x/day | at most x/day | at least x/day |
|---|---|---|---|
| 4 | 4.95 | 98.46 | 6.49 |
| 5 | 0.43 | 98.89 | 1.54 |
| 6 | 0.71 | 99.60 | 1.11 |
| 7 | 0.10 | 99.70 | 0.40 |
| 8 | 0.15 | 99.85 | 0.30 |
| 9 | 0.02 | 99.87 | 0.15 |
| 10 | 0.03 | 99.90 | 0.13 |
| 11 | 0.01 | 99.91 | 0.10 |
| 12 | 0.02 | 99.93 | 0.09 |
| ≥13 | 0.07 | 100.00 | 0.07 |

On average, patients prescribed Symbicort SMART in normal clinical practice used 3 Symbicort Turbuhaler inhalations in total per day (maintenance and as-needed inhalations). Patients used, on average, 0.8 as-needed inhalations per day, compared to 1.0 in the clinical study programme. On most of the days, patients required no as-needed inhalations, and the use of a high number of as-needed inhalations was restricted to few occasions. More than 6 as-needed inhalations were used on only 0.4% of the treatment days, compared to 0.8% in the clinical study programme, and more than 10 as-needed inhalations were used on 0.1% of the treatment days, compared to <0.1% in the clinical study programme. There was no indication that patients stopped or reduced their maintenance treatment or increased their as-needed use of Symbicort over time.