

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

***APPLICATION NUMBER:***

**NDA 20-441/S-016**

***Trade Name:*** Pulmicort Turbuhaler

***Generic Name:*** budesonide inhalation powder

***Sponsor:*** Astra Zeneca, LP

***Approval Date:*** October 24, 2003

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**NDA 20-441/S-016**

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### **Reviews / Information Included in this NDA Review.**

<b>Approval Letter</b>	<b>X</b>
<b>Approvable Letter</b>	
<b>Final Printed Labeling</b>	<b>X</b>
<b>Medical Review(s)</b>	
<b>Chemistry Review(s)</b>	
<b>EA/FONSI</b>	
<b>Pharmacology Review(s)</b>	
<b>Statistical Review(s)</b>	
<b>Microbiology Review(s)</b>	
<b>Clinical Pharmacology/ Biopharmaceutics Review(s)</b>	
<b>Administrative and Correspondence Document(s)</b>	<b>X</b>

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*

**NDA 20-441/S-016**

**APPROVAL LETTER**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 20-441/S-016

AstraZeneca LP  
1800 Concord Pike  
P.O. Box 8355  
Wilmington, DE 19803-8355

Attention: Christopher M. Blango  
Regulatory Affairs Director

Dear Mr. Blango:

Please refer to your supplemental new drug application dated February 28, 2002, received March 1, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pulmicort Turbuhaler (budesonide inhalation powder).

This "Changes Being Effectuated" supplemental new drug application provides for adding the target fill weight to the carton and updating the patient instruction portion of the label 200- dose packaging for consistency with the approved 60-dose packaging.

We completed our review of this supplemental new drug application. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on February 28, 2002.

We remind you that you must submit patent information on form FDA 3542, *Patent Information Submitted Upon and After Approval of an NDA or Supplement*, within 30 days of the date of this letter as required by 21 CFR 314.53(c)(2)(ii) and 314.53(d)(2) at the address provided by 21 CFR 314.53(d)(4). The form may be obtained at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>. To expedite review of this patent declaration form, we request you submit an additional copy of the form to this application and to the Center for Drug Evaluation and Research "Orange Book" staff at

Food and Drug Administration  
Office of Generic Drugs, HFD-610  
Orange Book Staff  
7500 Standish Place  
Metro Park North II  
Rockville, MD 20855-2773

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If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Colette Jackson, Regulatory Project Manager, at (301) 827-5584.

Sincerely,

*{See appended electronic signature page}*

Badrul A. Chowdhury, M.D., Ph.D.  
Division Director  
Division of Pulmonary and Allergy Drug Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

Enclosure

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**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
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/s/

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Badrul Chowdhury  
10/24/03 11:03:54 AM

**CENTER FOR DRUG EVALUATION AND RESEARCH**

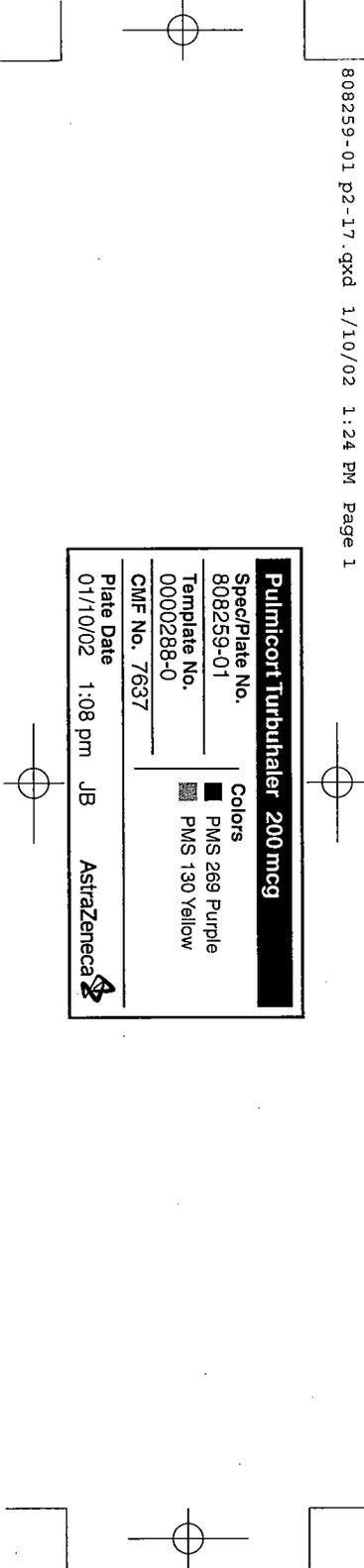
*APPLICATION NUMBER:*

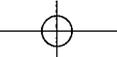
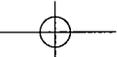
**NDA 20-441/S-016**

**APPROVED LABELING**

**Pulmicort Turbuhaler 200mcg**

Spec/Plate No. 808259-01	Colors
Template No. 0000288-0	■ PMS 269 Purple ■ PMS 130 Yellow
CMF No. 7637	
Plate Date 01/10/02 1:08 pm	JB
AstraZeneca 	



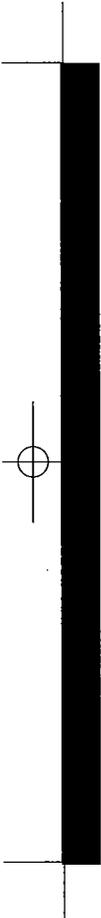


**Pulmicort**  
**200 mcg**  
200 Metered Doses

**Timbrehaler**  
(budesonide inhalation powder)  
NDC 0186-0915-42  
For Oral Inhalation. **Rx only**  
Store at 20–25°C (68–77°F) (see USP).  
**HOW TO USE PULMICORT TURBUHALER:** Refer inside to  
Patient's instructions for Use for additional information  
(including priming information).  
Do not remove the leaver until you have finished the medication.  
Manufactured for: AstraZeneca LP, Wilmington, DE 19850  
By: AstraZeneca AB, Södertälje, Sweden  
AstraZeneca

Asterisk reserved for  
supplier logo

80825901  
To Open: Peel back  
top corner of label.



# Pulmicort

**TURBUHALER**  
(budesonide inhalation powder)

**200 mcg**

200 Metered Doses  
For Oral Inhalation. Rx only

48139

808259-01

NDC 0186-0915-42  
Store at 20-25°C (68-77°F) (see USP)  
**HOW TO USE PULMICORT TURBUHALER:** Refer to Patient's Instructions for Use for additional information (including printing information).  
**Loading a Dose:** Twist cover and fill off. Hold inhaler upright (mouthpiece up). Turn brown grip fully to right. Twist it back again fully to left. You will hear the dose being loaded.  
**Inhaling the Dose:** Place mouthpiece between lips. Inhale deeply and forcefully. For more than one dose, repeat process. Place cover back on inhaler and twist shut. Rinse mouth with water. Keep inhaler clean and dry.  
Manufactured for: AstraZeneca LP Wilmington, DE 19850  
By: AstraZeneca AB, Södertälje, Sweden  
AstraZeneca

**REMEMBER:** This medicine has been prescribed for you by your doctor. DO NOT give this medicine to anyone else.

**USE THIS PRODUCT AS DIRECTED, UNLESS INSTRUCTED TO DO OTHERWISE BY YOUR DOCTOR.**

**If you have further questions about the use of PULMICORT TURBUHALER, call: 1-800-237-6898**

Extended Tak™ INCIB™ UK Pat. Nos. 8018923.3 & 9400832.3; Euro Pat. Nos. 91915912.8 & 94200154.6; US Pat. No. 5599403  
PULMICORT TURBUHALER is a trademark of the AstraZeneca group. © AstraZeneca 2001 808259-01 Rev. 12/01

AstraZeneca

83416 18

**WHAT YOU SHOULD KNOW ABOUT PULMICORT TURBUHALER®**

Your doctor has prescribed PULMICORT TURBUHALER 200 mcg. It contains a medication called budesonide, which is a synthetic corticosteroid. Corticosteroids are natural substances found in the body that help fight inflammation. They are used to treat asthma because they reduce the swelling and irritation in the walls of the small air passages in the lungs and ease breathing problems. When inhaled regularly, corticosteroids also help to prevent attacks of asthma. PULMICORT TURBUHALER treats the inflammation—the “quiet part” of asthma that you cannot hear, see, or feel. When inflammation is left untreated, your asthma symptoms and attacks can increase. PULMICORT TURBUHALER works to prevent and reduce your asthma symptoms and attacks.

page 3

- When the red mark reaches the bottom of the window, your inhaler should be discarded as it may no longer deliver the correct amount of medication. (You may still hear a sound if you shake it—this sound is not the medicine. This sound is produced by the drying agent inside the Turbuhaler.)
- Do not immerse it in water to find out if it is empty. Simply check your dose indicator window.

**FURTHER INFORMATION ABOUT PULMICORT TURBUHALER**

- PULMICORT TURBUHALER delivers your medicine as a very fine powder that you may not taste, smell, or feel. By following the instructions for use in this leaflet, you can be confident that you have received the correct dose.

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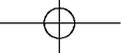
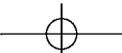
- 
- 
- 5 This medicine is NOT intended to provide rapid relief of your breathing difficulties during an asthma attack. It must be taken at regular intervals as recommended by your doctor, and not as an emergency measure.
  - 6 Your doctor may prescribe additional medication (such as bronchodilators) for emergency relief if an acute asthma attack occurs. Please contact your doctor if:
    - an asthma attack does not respond to the additional medication,
    - you require more of the additional medication than usual.
  - 7 If you also use another medicine by inhalation, you should consult your doctor for instructions on when to use it in relation to using your PULMICORT TURBUHALER.

Figure 5



**STORING YOUR PULMICORT TURBUHALER**

- After each use, place the white cover back on and twist it firmly into place.
- Keep PULMICORT TURBUHALER in a dry place at controlled room temperature, 68–77°F (20–25°C).
- Keep your PULMICORT TURBUHALER out of the reach of young children.
- DO NOT use after the date shown on the body of your Turbuhaler.



Figure 14



**USING YOUR PULMICORT TURBUHALER**

- Follow the instructions shown in the section "HOW TO USE YOUR PULMICORT TURBUHALER". If you have any problems, tell your doctor or pharmacist.
- It is important that you inhale each dose as directed by your doctor. The pharmacy label will usually tell you what dose to take and how often. If it doesn't, or you are not sure, ask your doctor or pharmacist.

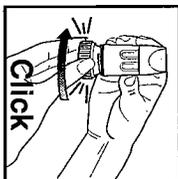
page 7

- You will hear a click.

**2 INHALING THE DOSE**

- When you are inhaling, PULMICORT TURBUHALER must be held in the upright (mouthpiece up) or horizontal position.
- Turn your head away from the inhaler and breathe out. Do not shake the inhaler after loading it.
- Place the mouthpiece between your lips and inhale deeply and forcefully. You may not taste or feel the medication.

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- It may take 1 to 2 weeks or longer before you feel maximum improvement, so IT IS VERY IMPORTANT THAT YOU USE PULMICORT TURBUHALER REGULARLY. DO NOT STOP TREATMENT OR REDUCE YOUR DOSE EVEN IF YOU ARE FEELING BETTER, unless told to do so by your doctor.
- If you miss a dose, just take your regularly scheduled next dose when it is due. **DO NOT DOUBLE** the dose.

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#### HOW TO USE YOUR PULMICORT TURBUHALER

Read the complete instructions carefully and use only as directed.

##### PRIMING INSTRUCTIONS:

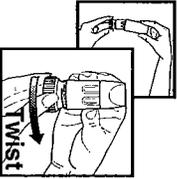
Before you use a new PULMICORT TURBUHALER for the first time, you should prime it. To do this, turn the cover and lift off. Hold PULMICORT TURBUHALER upright (with mouthpiece up), then twist the brown grip fully to the right and back again to the left. Repeat. Now you are ready to take your first dose (see instructions for "TAKING A DOSE"). You do not have to prime it any other time after this, even if you put it aside for a prolonged period of time.

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**TAKING A DOSE:**

**1 LOADING A DOSE**

- Twist the cover and lift off.
- In order to provide the correct dose, PULMICORT TURBUHALER **must be held in the upright position (mouthpiece up) whenever a dose of medication is being loaded.**
- Twist the brown grip fully to the right as far as it will go. Twist it back again fully to the left.



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**DOSAGE**

- Use as directed by your doctor.
- It is **VERY IMPORTANT** that you follow your doctor's instructions as to how many inhalations to take and how often to use your PULMICORT TURBUHALER.
- **DO NOT** inhale more doses or use your PULMICORT TURBUHALER more often than your doctor advises.

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- Do not chew or bite on the mouthpiece.
- Remove the inhaler from your mouth and exhale. Do not blow or exhale into the mouthpiece.
- If more than one dose is required, just repeat the steps above.
- When you are finished, place the cover back on the inhaler and twist shut. Rinse your mouth with water. Do not swallow.
- Keep your PULMICORT TURBUHALER clean and dry at all times.
- Do not use PULMICORT TURBUHALER if it has been damaged or if the mouthpiece has become detached.

FIGURE 13



**BEFORE USING YOUR PULMICORT TURBUHALER**

**TELL YOUR DOCTOR BEFORE STARTING TO TAKE THIS MEDICINE:**

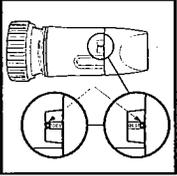
- if you are pregnant (or intending to become pregnant),
  - if you are breast-feeding a baby,
  - if you are allergic to budesonide or any other orally inhaled corticosteroid.
- In some circumstances, this medicine may not be suitable and your doctor may wish to give you a different medicine. Make sure that your doctor knows what other medicines you are taking.

FIGURE 5

**HOW TO KNOW WHEN YOUR PULMICORT  
TURBUHALER IS EMPTY**

The label on the box or cover will tell you how many doses are in your PULMICORT TURBUHALER. Your PULMICORT TURBUHALER has a convenient dose indicator window just below the mouthpiece.

- When a red mark appears at the top of the window, there are 20 doses of medicine remaining. Now is the time to get your next PULMICORT TURBUHALER.



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**IMPORTANT POINTS TO REMEMBER ABOUT PULMICORT TURBUHALER**

- 1 MAKE SURE that this medicine is suitable for you (see "BEFORE USING YOUR PULMICORT TURBUHALER").
- 2 It is important that you inhale each dose as your doctor has advised.
- 3 Use your Turbuhaler as directed by your doctor. **DO NOT STOP TREATMENT OR REDUCE YOUR DOSE EVEN IF YOU FEEL BETTER**, unless told to do so by your doctor.
- 4 **DO NOT** inhale more doses or use your Turbuhaler more often than instructed by your doctor.

Page 4

- PULMICORT TURBUHALER should not be used with a spacer.
  - PULMICORT TURBUHALER contains only budesonide and does not contain any inactive ingredients.
  - PULMICORT TURBUHALER is specially designed to deliver only one dose at a time, no matter how often you click the brown grip. If you accidentally blow into your inhaler after loading a dose, simply follow the instructions for loading a new dose.
- This leaflet does not contain the complete information about your medicine. If you have any questions, or are not sure about something, then you should ask your doctor or pharmacist. You may want to read this leaflet again. Please DO NOT THROW IT AWAY until you have finished your medicine.

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## Patent's Instructions for Use

**Pulmicort**  
**TURBUHALER** 200mg  
(budesonide inhalation powder)

Please read this leaflet carefully before you start to take your medicine. It provides a summary of information on your medicine.  
**FOR FURTHER INFORMATION ASK YOUR DOCTOR OR PHARMACIST.**

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**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*

**NDA 20-441/S-016**

**ADMINISTRATIVE DOCUMENTS**  
**AND**  
**CORRESPONDENCE**

Project Manager Labeling Review

NDA 20-441/S-016

DRUG: Pulmicort Turbuhaler (budesonide inhalation powder)

SPONSOR: AstraZeneca

SUBMISSION DATED: February 28, 2002 RECEIVED: March 01, 2002

This changes being effected supplemental application provides for revisions to the 200-dose trade packaging to make it consistent with the approved 60-dose packaging, by adding the target fill weight to the carton and by updating the patient instruction portion of the label, as committed to in a May 11, 2001 submission.

I compared the labeling dated February 28, 2002, to the last approved labeling (Approved December 31, 2001) and there are no changes other than those requested by this supplement. This supplement should be approved.

Sandy Barnes  
Chief, Project Management Staff  
Division of Pulmonary and Allergy Drug Products

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/s/

-----  
Sandra Barnes  
10/24/03 09:26:24 AM  
CSO

Craig Bertha  
10/24/03 09:44:00 AM  
CHEMIST  
I concur.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA20-441

**CBE-0 SUPPLEMENT**

AstraZeneca LP  
1800 Concord Pike, P. O. Box 8355  
Wilmington, DE 19803-8355  
Attention: Christopher M. Blango

Dear Mr. Blango:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Pulmicort Turbuhaler®(budesonide inhalation powder)

NDA Number: 20-441

Supplement number: SLR-016

Date of supplement: February 28, 2002

Date of receipt: March 04, 2002

This supplemental application was submitted as a "Supplement - Changes Being Effected." The appropriateness of reporting the proposed change(s) as changes being effected is under review.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on April 30, 2002 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:

Center for Drug Evaluation and Research  
Division of Pulmonary and Allergy Drug Products, HFD-570  
Attention: Division Document Room, 10B-03  
5600 Fishers Lane  
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Pulmonary and Allergy Drug Products

NDA-20-441/S-016

Page 2

Attention: Document Room 10B-03

5600 Fishers Lane

Rockville, Maryland 20857

If you have any question, call Anthony Zeccola, Regulatory Management Officer, at (301) 827-1058.

Sincerely yours,

Sandra L. Barnes  
Chief, Project Management Staff  
Division of Pulmonary and Allergy Drug Products  
Office of Drug Evaluation ii  
Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
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/s/

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Anthony Zeccola

3/7/02 02:07:28 PM

Signed by Anthony Zeccola for Sandra Barnes