CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:
NDA 20-441/S010

Trade Name: Pulmicort Turbuhaler

Generic Name: budesonide inhalation powder, 200 mcg

Sponsor: Astra Pharmaceuticals

Approval Date: July 7, 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 20-441/S010

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 20-441/S010

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-441/S-010

AstraZeneca LP
725 Chesterbrook Blvd.
Wayne, PA 19087-5677

Attention: Eric Couture, Ph.D.
Director, Regulatory Affairs

Dear Dr. Couture:

Please refer to your supplemental new drug application dated December 22, 2000, received December 26, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pulmicort (budesonide) Inhalation Powder.

We acknowledge receipt of your submissions dated May 11, and September 11, and 17, 2001. Your submission of September 11, 2001, constituted a complete response to our July 9, 2001, action letter.

This supplemental new drug application provides for a new 60-dose unit for Pulmicort Turbuhaler with the M0-ESP formulation and 200 mcg/dose configuration.

We have completed the review of this supplemental application, and it is approved.

We remind you of your commitment to take measures to improve the product performance as listed in your June 6, 1997, amendment and the Agency concerns regarding the unacceptably slow progress in the implementation as outlined in comment 1 of the March 12, 2001, approvable letter and comment 2 of the July 9, 2001, approvable letter.

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 Ms. Ladan Jafari, Regulatory Project Manager, at (301) 827-5584.

Sincerely,

{See appended electronic signature page}

Guirag Poochikian, Ph.D.
Chemistry Team Leader
Division of Pulmonary and Allergy Drug Products, HFD-570
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Guiragos Poochikian
10/15/01 04:47:44 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-441/S010

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service
Food and Drug Administration
Rockville MD 20857

NDA 20-441/S-010

AstraZeneca LP
P.O. Box 8355
Wilmington DE 19803-8355

Attention: Eric Couture, Ph.D.
Director, Regulatory Affairs

Dear Dr. Couture:

Please refer to your supplemental new drug application dated December 22, 200, received December 26, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pulmicort Turbuhaler (budesonide inhalation powder).

We acknowledge receipt of your submission dated May 11, 2001. Your submission of May 11, 2001, constituted a complete response to our March 12, 2001, action letter.

This supplement proposes a new 60-dose unit for the Pulmicort Turbuhaler M0-ESP, 200 mcg/60 doses.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to address the following deficiencies.

1. Revise the last paragraph of the DESCRIPTION section in the labeling as follows:

   In vitro testing has shown that the dose delivery for the PULMICORT TURBUHALER is —— substantially dependent on air flow through the device. ——, patient factors, such as inspiratory flow rates, will affect the dose delivered to the lungs of patients in actual use (see Patient's Instructions for Use). In adult patients with asthma (mean $FEV_1$2.9L[0.8-5.1L]) mean peak inspiratory flow (PIF) through PULMICORT TURBUHALER was 78 (40-111)L/min. Similar results (mean PIF 82[43-125]L/min) were obtained in asthmatic children (6 to 15 years, mean $FEV_1$2.1L[0.9-5.4L]). Patients should be carefully instructed on the use of this drug product to assure optimal dose delivery.

2. We remind you of your agreement regarding improvement of the Pulmicort Turbuhaler performance characteristics, as listed in your June 6, 1997, amendment and the Agency concerns regarding the unacceptably slow progress in the implementation as outlined in comment 1 of the March 12, 2001, approvable letter. You should commit adequate resources for expeditious improvement of the product performance. Provide a revised timeline for the final implementation of the product improvements.

To facilitate review of your submission, please provide a highlighted or marked-up copy of the labeling that shows the changes that are being made.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with this change prior to approval of this supplemental application.

If you have any questions, call Gretchen Trout, Project Manager, at (301) 827-1058.

Sincerely yours,

{See appended electronic signature page}

Guirag Poochikian, Ph.D.
Chemistry Team Leader
Division of Pulmonary and Allergy Drug Products, HFD-570
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Brian Rogers
7/9/01 11:00:34 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-441/S-010

AstraZeneca LP
P.O. Box 8355
Wilmington, DE 29803-8355

Attention: Eric Couture, Ph.D.
Director, Regulatory Affairs

Dear Dr. Couture:

Please refer to your supplemental new drug application dated December 22, 2000, received December 26, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pulmicort Turbuhaler (budesonide inhalation powder).

This supplement proposes the following change: a new 60-dose unit for the Pulmicort Turbuhaler M0-ESP 200 mcg/dose.

We have completed the review of this application, and it is approvable. Before this application may be approved, however, it will be necessary for you to address the following:

1. We remind you of your agreement regarding improvement of the Pulmicort Turbuhaler performance characteristics, as listed in your June 6, 1997, amendment; i.e., you will conduct an ongoing development program for Turbuhaler which includes modifications of Turbuhaler, the process of [redacted] micronized budesonide, the powder composition, and possible clinical testing.

   It was expected that a revised Pulmicort Turbuhaler drug product, which meets the Agency expectations for dose delivery and particle size distribution, would have been realized by now, considering the substantial time period since your original commitment. Yet, during our review of the submissions supporting the 60 and 200 count M0-ESP products, it was noted that the dose delivery data are still [redacted] not to mention that the [redacted]
   Inform the Agency of improvements of the Pulmicort Turbuhaler in terms of dose delivery and aerodynamic particle size distribution that meet the Agency's expectations and provide the implementation date for these improvements.

2. Provide a comprehensive summary of what measures and associated acceptance specifications are in place that assure your ability to distinguish (e.g., examinations of markings, dimensional measurements) the 60 count and 200 count device components containing the dosing units and the filled but unlabeled devices, to prevent potential confusion or mixing prior to labeling and packaging.

3. Provide the composition (additives, colorants, residual catalyst levels, etc.)

Confirm that this material is currently being manufactured and supply all of the pertinent information by reference to a drug master file.

4. The following comments pertain to the labels and labeling.

   a. Due to the high dependence of the dose delivery of the product on the flow rate, as evidenced by your *in vitro* testing at flow rates of 40, 60, and 80 L/min, the DESCRIPTION section of the labeling should be revised to clearly indicate this important characteristic of the product for the prescribing physicians.

   b. The HOW SUPPLIED section and the "contents" statement on the carton should include the fill weight of the reservoir.

   c. The HOW SUPPLIED section should include a description of the device indicator which signals the number of remaining doses.

   d. The HOW SUPPLIED section and the PATIENT PACKAGE INSERT should include a warning to the patient that if the unit is used beyond the point at which the red mark appears at the bottom of the window, the correct amount of medication may not be obtained from the product.

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Food and Drug Administration
Rockville MD 20857

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with this change prior to approval of this supplemental application.

If you have any questions, call Gretchen Trout, Project Manager, at (301) 827-1058.

Sincerely yours,

{See appended electronic signature page}

Guirag Poochikian, Ph.D.
Chemistry Team Leader
Division of Pulmonary and Allergy Drug Products
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

/s/

Guiragos Poochikian
3/12/01 01:27:44 PM

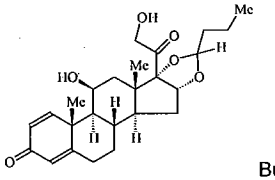
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-441/S010

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW #3

	1. ORGANIZATION HFD-570 DPADP	2. NDA NUMBER 20-441
3. NAME AND ADDRESS OF APPLICANT *(City and State)* AstraZeneca LP 725 Chesterbrook Blvd Wayne, PA 19087-5677		4. AF NUMBER 5. SUPPLEMENT(S) NUMBER(S) DATES(S) SCP-010 12/22/00
6. NAME OF DRUG Pulmicort® Turbuhaler®	7. NONPROPRIETARY NAME budesonide inhalation powder	
8. SUPPLEMENT PROVIDES FOR: A new 60-dose unit for Pulmicort Turbuhaler with the M0-ESP formulation and 200 mcg/dose configuration.		9. AMENDMENT(S), REPORT(S), ETC. C 1/15/01 SCP-010 AC 5/11/01 SCP-010 AC 9/11/01* SCP-017 BC 9/17/01* C 8/30/01* *subject of this review
10. PHARMACOLOGICAL CATEGORY steroid anti-inflammatory	11. HOW DISPENSED RX X OTC __	12. RELATED IND/NDA/DMF
13. DOSAGE FORM(S) inhalation powder	14. POTENCY 200 mcg metered; as noted in S-009,	
15. CHEMICAL NAME AND STRUCTURE  Budesonide or (*RS*)-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with butyraldehyde		16. RECORDS AND REPORTS CURRENT YES__NO___ REVIEWED YES__NO___

17. COMMENTS: See review notes attached.

cc:
Orig. NDA 20-441
HFD-570/div. File
HFD-570/CBertha/9/20/01
HFD-570/GPoochikian
HFD-570/LJafari
R/D Init. by:_____
F/T by: CBertha/9/20/01
doc # 01-09-17.rev.doc

18. CONCLUSIONS AND RECOMMENDATIONS: From the CMC perspective it is recommended that the supplement be **approved (AP)**. The comment in the draft letter should be forwarded in the approval letter to the applicant.

19. REVIEWER NAME:	SIGNATURE	DATE COMPLETED
Craig M. Bertha, Ph.D.		9/20/01

5 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-441 / 5010
chem Rev. #3

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/s/

Craig Bertha
9/25/01 06:31:03 AM
CHEMIST

Guiragos Poochikian
9/25/01 06:25:11 PM
CHEMIST

CHEMIST'S REVIEW #2

1. ORGANIZATION	2. NDA NUMBER
HFD-570 DPADP	20-441

3. NAME AND ADDRESS OF APPLICANT *(City and State)*
AstraZeneca LP
725 Chesterbrook Blvd
Wayne, PA 19087-5677

4. AF NUMBER

5. SUPPLEMENT(S)
NUMBER(S) DATES(S)
SCP-010 12/22/00

6. NAME OF DRUG	7. NONPROPRIETARY NAME
Pulmicort® Turbuhaler®	budesonide inhalation powder

8. SUPPLEMENT PROVIDES FOR: A new 60-dose unit for Pulmicort Turbuhaler with the M0-ESP formulation and 200 mcg/dose configuration.

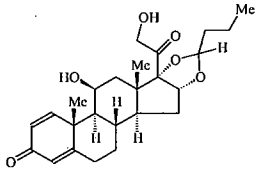
9. AMENDMENT(S), REPORT(S), ETC.

C 1/15/01
SCP-010 AC 5/11/01*
*subject of this review

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF
steroid anti-inflammatory	RX X OTC __	

13. DOSAGE FORM(S)	14. POTENCY
inhalation powder	200 mcg metered; as noted in S-009,

15. CHEMICAL NAME AND STRUCTURE



Budesonide or (*RS*)-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with butyraldehyde

16. RECORDS AND REPORTS
CURRENT YES__NO___
REVIEWED YES__NO___

17. COMMENTS: See review notes attached.

cc:
Orig. NDA 20-441
HFD-570/div. File
HFD-570/CBertha/6/28/01
HFD-570/GPoochikian
HFD-570/GTrout
R/D Init. by:_____
F/T by: CBertha/6/28/01
doc # 01-05-11.rev.doc

18. CONCLUSIONS AND RECOMMENDATIONS: From the CMC perspective, the supplement is **approvable (AE)**. The comment, resulting from the internal meeting within HFD-570 on 6/15/01, included in the attached draft letter as #2, should be forwarded to the applicant with the action letter. With comment #1 of the draft letter, the applicant will also be reminded of their commitment for improvement of the performance characteristics of the inhalers as outline in their June 6, 1997 amendment.

19. REVIEWER NAME:	SIGNATURE	DATE COMPLETED
Craig M. Bertha, Ph.D.		6/28/01

10 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-441
5010
Chem Rev. #2

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/s/

Craig Bertha
6/28/01 10:12:49 AM
CHEMIST

Guiragos Poochikian
6/28/01 04:23:05 PM
CHEMIST

CHEMIST'S REVIEW #1

1. ORGANIZATION	2. NDA NUMBER
HFD-570 DPADP	20-441

3. NAME AND ADDRESS OF APPLICANT *(City and State)*
AstraZeneca LP
725 Chesterbrook Blvd
Wayne, PA 19087-5677

4. AF NUMBER

5. SUPPLEMENT(S)
NUMBER(S) DATES(S)
SCS-010 12/22/00

6. NAME OF DRUG	7. NONPROPRIETARY NAME
Pulmicort® Turbuhaler®	budesonide inhalation powder

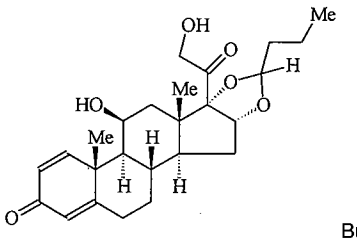
8. SUPPLEMENT PROVIDES FOR: A new 60-dose unit for Pulmicort Turbuhaler with the M0-ESP formulation and 200 mcg/dose configuration.

9. AMENDMENT(S), REPORT(S), ETC.
C 1/15/01

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF
steroid anti-inflammatory	RX X OTC __	

13. DOSAGE FORM(S)	14. POTENCY
inhalation powder	200 mcg metered; as noted in S-009.

15. CHEMICAL NAME AND STRUCTURE



Budesonide or (*RS*)-11β,16α,17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with butyraldehyde

16. RECORDS AND REPORTS
CURRENT YES__NO___
REVIEWED YES__NO___

17. COMMENTS: See review notes attached.

cc:
Orig. NDA 20-441
HFD-570/div. File
HFD-570/CBertha/2/12/01
HFD-570/GPoochikian
HFD-570/GTrout
R/D Init. by:_____
F/T by: CBertha/2/12/01
doc # 00-12-22.rev.doc

NOTE THAT THE METHOD VALIDATION INFORMATION ASSOCIATED WITH THE PRODUCT SUBMITTED WITH S-009 AND S-010 HAS NOT BEEN REVIEWED SINCE IT IS NOT RELATED TO THE SUBJECT OF EITHER SUPPLEMENT. THIS INFORMATION WILL BE REVIEWED SEPARATELY.

18. CONCLUSIONS AND RECOMMENDATIONS: From the CMC perspective, the supplement is **approvable (AE)**. The comments in the attached draft letter should be forwarded to the applicant.

19. REVIEWER NAME:	SIGNATURE	DATE COMPLETED
Craig M. Bertha, Ph.D.		2/12/01

56 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 20-441
5010
Chem Rev. #1

/s/

Craig Bertha
2/12/01 02:31:21 PM
CHEMIST

Guiragos Poochikian
2/12/01 05:18:36 PM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-441/S010

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Memorandum of Telephone Facsimile Correspondence

Date: May 30, 2001

To: Eric Couture
Director, Regulatory Affairs

Fax: 610-722-7784

From: Gretchen Trout
Project Manager

Subject: NDA 20-441/S-010
May 1, 2001, Meeting/teleconference

Reference is made to the meeting/teleconference held between representatives of your company and this Division on May 1, 2001. Attached is a copy of our final minutes for that meeting/teleconference. These minutes will serve as the official record of the meeting/teleconference. If you have any questions or comments regarding the minutes, please call me at (301) 827-1058.

Thank you.

MINUTES OF INDUSTRY TELECONFERENCE

DATE: May 1, 2001

NDA 20-441/S-010

PRODUCT: Pulmicort Turbuhaler

FDA Participants:

Craig Bertha, Chemistry Reviewer
Guirag Poochikian, Chemistry Team Leader
Gretchen Trout, Project Manager

AstraZeneca Participants:

Eric Couture, director, Regulatory Affairs
Liuda Shtohyrn, Associate Director, Technical Regulatory Affairs
Ann Smith, Sr. Manager, Operations CMC Strategy
James Sullivan, Regulatory Project Manager

BACKGROUND: On March 12, 2001, the Division issued an approvable letter for S-010. Dr. Couture telephoned Mrs. Trout on March 29, 2001, and asked for clarifications on comments 1, 4.a., and 4.b., from the March 12, 2001, letter. The Division scheduled a teleconference to address AstraZeneca's questions.

In comment 1 of the letter, the Division stated that the fine particle dose is still observed to [redacted] AstraZeneca questioned if this refers to within [redacted] The Division informed AstraZeneca that our comment was referring to within [redacted]

In comment 4.a., the Division had stated that the DESCRIPTION section of the labeling should be revised to indicate the dependence of the dose delivery on the flow rate. AstraZeneca pointed out that they already have language in the package insert that states that "the mount of drug delivered to the lung will depend on patient factors..."

[redacted] the language should be amplified and should be more clear for physicians and patients. [redacted]

[redacted] AstraZeneca raised the issue of standard deviation. The Division stated that if the standard deviation is large, [redacted]

that might be acceptable. The Division stated that we would even be willing to go up to 10%.

The Division replied that it is difficult to assess. The Division suggested that AstraZeneca consider our comments and propose language to address the issue in the package insert, the Division will consider what AstraZeneca proposes. The Division pointed out that the variability in dose delivery has been an issue since this product was approved, and that the understanding was that this would be resolved quickly. AstraZeneca stated that they are

For comment 4.b. the Division requested that AstraZeneca include the fill weight of the reservoir in the HOW SUPPLIED section. AstraZeneca questioned if the Division wanted the target fill weight. The Division informed AstraZeneca that the target fill weight is adequate for the container label and the package insert.

This addressed all of AstraZeneca's comments/concerns from the Approvable letter.

Rd initial by: Bertha/5-21-01

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/s/

Gretchen Trout
5/30/01 10:33:26 AM
CSO

MEMORANDUM: DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: March 20, 2001

TO: N 20-441 File, Pulmicort Turbuhaler (budesonide inhalation powder)

THROUGH: Guirag Poochikian, Ph.D.
Chemistry Team Leader
Division of Pulmonary Drug Products (HFD-570)

FROM: Craig M. Bertha, Ph.D.
Chemistry Reviewer
Division of Pulmonary Drug Products (HFD-570)

SUBJECT: Field alert report from AstraZeneca dated 3/16/01

BACKGROUND: Pulmicort Turbuhaler product formulated as M0 and the M0-ESP version approved in S-009 was known by Agency to provide occasional doses. The applicant is still in the process of developing the product further to lessen dosing variability particle size distribution. For example, from the recent AE letter dated 3/12/01 for S-010, the Agency summarized the following.

"We remind you of your agreement regarding improvement of the Pulmicort Turbuhaler performance characteristics, as listed in your June 6, 1997, amendment; i.e., you will conduct an ongoing development program for Turbuhaler which includes modifications of Turbuhaler, the process budesonide, the powder composition, and possible clinical testing.

It was expected that a revised Pulmicort Turbuhaler drug product, which meets the Agency expectations for dose delivery and particle size distribution, would have been realized by now, considering the substantial time period since your original commitment. Yet, during our review of the submissions supporting the 60 and 200 count M0-ESP products, it was noted that the dose delivery data are still quite variable

Inform the Agency of improvements of the Pulmicort Turbuhaler in terms of dose delivery and aerodynamic particle size distribution that meet the Agency's

expectations and provide the implementation date for these improvements."

CONTENT: The report from AZ dated 3/16/01 indicates that for their post-production stability program for the product, sub-batch 04 of lot BH1195, which had been stored on stability for three months under conditions of / , / had a mean delivered dose for the 1st tier testing (n = 10 units) of 185 mcg/dose. This value is just above the 115% upper limit relative to label claim of 184 mcg/dose. AZ has not attributed this result to laboratory error and will proceed with the tier 2 testing of 20 additional inhalers. Note that there is *not* a two-tiered mean for the release or stability testing of this product. AZ states that they will report the results of the additional testing on more samples from this stability sub-batch as soon as they are available.

From CR#1 for S-009 for the M0-ESP 200 count product, it was noted by the reviewer that / — / were seen for both the older M0 and the newer M0-ESP formulated product and that the "frequency and size / — / were similar. It was further elaborated that the "largest dose found for M0-ESP was / — / for M0) and that the possibility of occasional doses of up to / ng was assessed during review of the original NDA and found to be acceptable." Because of the previous Agency consideration of the / — / dosing behavior, the relatively small magnitude of the / —— / occurrence, combined with the Agency's continual prompting of the applicant to proceed with their development of a more well behaved product (in terms of dosing), no action will be recommended to be taken at this time regarding this field alert report. This position will be reassessed once the applicant has provided the Agency with the additional promised data on dose delivery for this stability sub-batch.

Craig M. Bertha, Ph.D.
Chemistry Reviewer

cc:
Orig. NDA 20-441
HFD-570/Div. Files
HFD-570/CBertha
HFD-570/GPoochikian
HFD-570/GTrout

/s/

Craig Bertha
3/21/01 06:56:06 AM
CHEMIST

See hardcopy in box BEFORE signing this.

Guiragos Poochikian
3/21/01 11:09:29 AM
CHEMIST

CSO LABELING REVIEW

NDA 20-441/SCP-010
Submission date: December 22, 2000

BACKGROUND: This supplement provides for a new 60-dose unit for Pulmicort Turbuhaler M0-ESP 200 mcg/dose with revisions to the HOW SUPPLIED section of the package insert, the Patients Instructions for Use, and new labels for the 60-dose unit.

I compared the package insert with the most recently approved package insert (S-002, approved October 8, 1998) and noted the following changes (in addition to the changes proposed with regard to the new 60-dose unit).

1. In the CLINICAL TRIALS section, ' ' was replaced with "asthma stability" as per the October 8, 1998, letter.
2. In the PRECAUTIONS section, the last sentence of the ' growth suppression (see PRECAUTIONS, Pediatric Use section). see PRECAUTIONS, Pediatric Use section)."

   Previously in the same paragraph, references were made to , therefore the new language is consistent with what was already in the label and is acceptable.

I also compared the Patient's Instructions for Use with the originally approved Patient's Instructions for Use and found no changes,

CONCLUSION: I found no changes in the label that would affect the approvability of this supplement. See Chemist's review dated February 12, 2001, for labeling comments that need to be conveyed to the sponsor.

/s/

Gretchen Trout
3/12/01 10:52:15 AM
CSO

Sandra Barnes
3/12/01 10:58:16 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-441/S-010

PRIOR APPROVAL SUPPLEMENT

AstraZeneca LP
P.O. Box 8355
Wilmington, DE 29803-8355

Attention: Eric Couture, Ph.D.
Director, Regulatory Affairs

Dear Dr. Couture:

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: S-010

Date of Supplement: December 22, 2000

Date of Receipt: December 26, 2000

This supplement proposes the following change(s): a new 60-dose unit for Pulmicort Turbuhaler M0-ESP 200 mcg/dose.

Unless we notify you within 60 days of our 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 February 24, 2001 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be April 24, 2001 and the secondary user fee goal date will be June 24, 2001.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary and Allergy Drug Products, HFD-570

Food and Drug Administration
Rockville MD 20857

Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call me at (301) 827-1058.

Sincerely yours,

Gretchen Trout
Project Manager
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

/s/

Gretchen Trout
1/9/01 01:21:48 PM