

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-247

PROPRIETARY NAME REVIEW(S)

**Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
WO22; Mail Stop 4447
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: November 1, 2005

NDA#: 21-247

NAME OF DRUG: **Aerospan HFA**
(Flunisolide Inhalation Aerosol)
80 mcg of flunisolide hemihydrate per actuation

NDA HOLDER: Forest Pharmaceuticals, Inc.

*****NOTE:** This review contains proprietary and confidential information that should not be released to the public.***

I. INTRODUCTION:

This consult was written in response to a request from the Division of Pulmonary and Allergy Products (HFD-570), for assessment of the proprietary name "Aerospan HFA", regarding potential name confusion with other proprietary or established drug names.

The proposed name, Aerospan, was found acceptable by DMETS in reviews dated May 8, 2003 (ODS consult #01-0050-2) and March 31, 2004 (ODS Consult #01-0050-3). Now, the sponsor has added "HFA" to the proposed tradename, as requested by the Review Division's CMC group. DMETS provided suggestions for improvement on the labels and labeling in the last review. Revised container labels, carton and insert labeling were provided for re-review and comment at this time. Many of the label and labeling comments provided in this review were included in ODS Consult 01-0050-3 dated March 31, 2004, but were not incorporated in the revised labels and labeling.

Forest Pharmaceuticals is the manufacturer for Aerospan and the currently marketed Aerobid. As per a discussion with the Division Project Manager, Aerospan will replace Aerobid once it is approved. Aerospan contains the same active ingredient as Aerobid, without the chlorofluorocarbon (CFC). As noted in a memorandum to the Division dated March 15, 2001, the average particle size of flunisolide hemihydrate in Aerospan is much smaller than the CFC flunisolide hemihydrate suspension formulation in Aerobid. As a result, the respirable fraction is higher than that in the CFC formulation. Thus, a lower total daily dose of Aerospan is needed to achieve the same effect as Aerobid.

PRODUCT INFORMATION

Aerospan HFA (Flunisolide Inhalation Aerosol) is indicated for the maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients six years of age and older. Aerospan HFA is also indicated for patients requiring oral corticosteroid therapy for asthma. Many of those patients may be able to reduce or eliminate their requirement for oral corticosteroids over time. Aerospan HFA is not indicated for the relief of acute bronchospasm. Flunisolide is a solution formulation that does not contain chlorofluorocarbons (CFCs) as the propellant. Aerospan HFA should be administered by the orally inhaled route in asthmatic patients aged 6 years and older. The recommended adult (12 and older) starting dose is 2 inhalations twice daily (morning and evening) and the maximum daily dose should not

exceed 4 inhalations twice daily. The recommended initial dose for children (age 6 to 11) is one inhalation twice daily (morning and evening), not to exceed a maximum dose of 2 inhalations twice daily. Higher doses in children have not been studied. Aerospan HFA is supplied as a pressurized aluminum canister with a two piece purple actuator/gray spacer assembly in one box. Each actuation delivers approximately 80 mcg flunisolide hemihydrate (equivalent to 78 mcg flunisolide) to the patient. Aerospan HFA will be available in an 8.9 gram (containing 120 inhalations) and a 5.1 gram (containing 60 inhalations) net weight canister.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2}, as well as several FDA databases³ for existing drug names which sound-alike or look-alike to Aerospan HFA to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁴. The Saegis⁵ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Aerospan HFA. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name, Aerospan HFA, acceptable from a promotional perspective.
2. The Expert Panel identified one additional proprietary name that was thought to have potential for confusion with Aerospan HFA. This product is listed in table 1 (see page 4), along with the dosage form and usual dosage.

¹ MICROMEDEX Integrated Index, 2005, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, 2005, Facts and Comparisons, St. Louis, MO.

³ The Division of Medication Errors and Technical Support [DMETS] database of proprietary name consultation requests, Drugs@FDA, and the electronic online version of the FDA Orange Book.

⁴ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

⁵ WWW location <http://www.uspto.gov/tmdb/index.html>.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by EPD

Product Name	Established name, Dosage form(s)	Usual adult dose*	Other
Aerospan HFA	Flunisolide Inhalation Aerosol, 80 mcg Flunisolide Hemihydrate per actuation	Treatment of asthma as prophylactic therapy in adults and pediatric patients six years of age and older: Adults: 2 inhalations twice daily, morning and evening (maximum daily dose is 4 inhalations twice daily) Ages 6 to 11: One inhalation twice daily, morning and evening (maximum daily dose is 2 inhalations twice daily)	
_____	Formoterol Fumarate, 2 mL sterile solution for nebulization	Maintenance treatment of bronchoconstriction in patients with COPD: 20 mcg every 12 hours	Look-alike, Sound-alike

*Frequently used, not all-inclusive.

NOTE: This review contains proprietary and confidential information that should not be released to the public.

B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. The POCA did not identify any additional names considered to have significant phonetic or orthographic similarities to Aerospan HFA.

C. PRESCRIPTION ANALYSIS STUDIES

Prescription studies were not performed for the proposed tradename, Aerospan HFA. Prescription studies had been conducted on the original proposed name, Aerospan. The sponsor proposes to add "HFA" to the name, and since HFA is the standard abbreviation for this type of product a study is not needed at this time.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proposed proprietary name Aerospan HFA, the primary concerns raised were related to look-alike confusion with _____ ***.

_____*** was identified to have look-alike potential with Aerospan HFA, if the HFA is inadvertently omitted from the name. _____ is the alternate proposed proprietary name for an IND (_____) indicated for the maintenance treatment of bronchoconstriction in patients with COPD. _____ is the primary proposed name for this IND application. Since _____ are in the initial stages of review with DMETS, it is premature at this point to determine which proposed proprietary name will be acceptable. _____ will be available as a 2 mL sterile solution for nebulization. The usual dose is 20 mcg every 12 hours. DMETS would like to comment that based on the information available at this time, we would have concern if both

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Aerospan HFA and _____ approved by the Agency, as the two have overlapping product and look-alike characteristics. Aerospan and _____ each have six identical beginning letters (“Aerosp”) and end with a similar looking letter (“n” vs. _____, when scripted _____ as one additional _____ le _____ towards the end of the name, but this may be easily overlooked as the beginning of each name is identical. Besides look-alike similarities, the two drugs have overlapping directions for use (2 inhalations BID vs. 2 mL BID), frequency of administration (twice daily), route of administration (oral inhalation/nebulization), and patient/prescriber population. In addition, _____ is indicated for the treatment of bronchoconstriction in patients with COPD and Aerospan is NOT indicated for the relief of acute bronchospasm. This difference in indication for use may be of safety concern if one drug is inadvertently administered instead of the other. DMETS has no objections to the use of the proposed proprietary name Aerospan HFA provided that only one name, Aerospan HFA (NDA 21-247) or _____) is approved.

Aerospan

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the re-review of the container labels, carton and insert labeling of Aerospan HFA, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS provided suggestions for improvement on the labels and labeling in the last review. Many of the label and labeling comments provided in this review were included in ODS Consult 01-0050-3 dated March 31, 2004, but were not incorporated in the revised labels and labeling. Additionally, DMETS has identified several additional areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

DMETS notes the use of trailing zeroes throughout the package insert labeling. For example, the Pharmacodynamics section of the CLINICAL PHARMACOLOGY section states, “Administration of flunisolide hemihydrate 2.0 mg twice daily....” The use of terminal zeroes may result in error as decimals are often overlooked. As evidenced by our post-marketing surveillance, the use of terminal zeroes could potentially result in a ten-fold medication dose error. The use of terminal zeroes in the expression of strength or volume is not in accordance with the General Notices (page 10) of 2004 USP, which states, “...to help minimize the possibility of error in the dispensing and administration of the drugs...the quantity of active ingredient when expressed in whole numbers shall be shown without a decimal point that is followed by a terminal zero.” In addition, the use of trailing zeroes is specifically listed as a dangerous abbreviation, acronym, or symbol in the 2006 National Patient Safety Goals of The Joint Commission for the Accreditation of Hospitals (JCAHO). Lastly, safety groups such as ISMP also list terminal zeroes on their dangerous abbreviations and dose designations list. Revise the labeling so that strengths, etc. are expressed without the use of a terminal zero (e.g., the dosage should read 2 mg instead of 2.0 mg).

B. CONTAINER LABELS

1. The product strength/actuation should be prominently placed on the principal display panel in conjunction with the proprietary name. Additionally, the statements “60 metered actuations” and “120 metered actuations” should be relocated to follow the strength on the principal display panel. For example, “The dose delivered per actuation from the mouthpiece is 80 mcg flunisolide hemihydrate. Contains 60 actuations per canister.”

2. DMETS recommends decreasing the size of net weight quantities, 5.1 g and 8.9 g, respectively, as the number of metered actuations is often used by practitioners to identify the quantity to be dispensed.
3. We recommend removing the "swoosh" from over the tradename Aerospan HFA as it distracts from the proprietary name.
4. The route of administration "For Oral Inhalation Only" should be prominently displayed on the principal display panel.

C. CARTON LABELING

1. We recommend increasing the prominence of the statement "PROFESSIONAL SAMPLE – NOT FOR RESALE".
2. See comments A1 – A4.

D. INSERT LABELING

1. PRECAUTIONS

Information for Patients

- a. The package insert states, "AEROSPAN HFA canister contains 120 actuations." Since Aerospan is available in different canister sizes, (8.9 grams and 5.1 grams), the statement should list the number of actuations for each canister size. This statement should also be revised in the PATIENT'S INSTRUCTIONS FOR USE.

2. DOSAGE AND ADMINISTRATION

Transferring Patients from Other Inhaled Steroids to AEROSPAN HFA:

- a. This section begins by stating "Patients who are controlled on other inhaled steroids..." We question whether "other inhaled steroids" means those inhaled steroids with CFC? Please comment.
- b. This section contains a dose conversion table from *Other Inhaled Steroids or Flunisolide CFC to AEROSPAN HFA*. DMETS believes the current dosing conversion table is confusing and recommends revising as follows for clarity.

Current Medication	Dose of Current Medication	HFA Equivalent Dose
Flunisolide CFC or Equivalent Oral Inhaled Corticosteroid	500 mcg BID	160 mcg BID
Flunisolide CFC or Equivalent Oral Inhaled Corticosteroid	1000 mcg BID	320 mcg BID

- c. In the table, the dose conversion is expressed in concentration (mcg) of the inhalation. In addition to the mcg, a column for number of inhalations per dose should be included to minimize the risk of potential miscalculation of number of inhalations to be used per dose.
- d. The paragraph following the table describes clinical trials performed in children ages 4-11 who successfully transferred from flunisolide CFC to flunisolide HFA. Since Aerospas HFA is indicated to treat children older than 6 years of age, this contradicts the recommended age group of children and may cause confusion. Please comment.

3. PATIENT'S INSTRUCTION FOR USE

- a. The first paragraph of the DIRECTIONS for USE section currently reads, "Before using new AEROSPAN HFA...." Revise line 679 to read, "Before using a new AEROSPAN HFA...." to avoid misunderstanding of the word "new".
- b. The third paragraph of the DIRECTIONS for USE section is numbered and the fourth bullet reads, "Check that the canister is fully seated in the actuator." To enhance clarity, please revise the sentence to read as follows, "Check that the canister is completely inserted into the actuator."
- c. Clarify the picture in Figure 1 by labeling the canister, mouthpiece and actuator.
- d. Bold the statement in Step 5 – Using Your Aerospas HFA which reads, "If you are using the inhaler for the first time, or if the inhaler has not been used for more than 2 weeks, you will need to prime (prepare) the inhaler" to ensure patients are aware of this important information.
- e. In Figure 11, delete the downward arrow shown. It indicates depressing the actuator, when the figure and narrative demonstrates placing the actuator in the mouth.

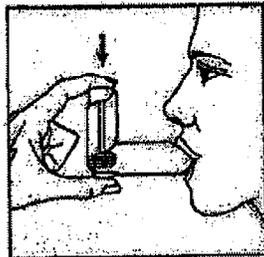


Figure 11

- f. Bold and highlight the word "Caution" in the warning statement following Step 10.
- g. In Figure 12, add a downward arrow to accentuate depressing the actuator.

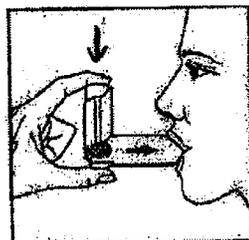


Figure 12

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

/s/

Nora L. Roselle
11/10/2005 03:42:13 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
11/10/2005 04:16:04 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
11/14/2005 12:52:10 PM
DRUG SAFETY OFFICE REVIEWER

CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)**

DATE RECEIVED: 12/11/03	DESIRED COMPLETION DATE: 3/15/04 PDUFA DATE: 4/20/04	ODS CONSULT #: 01-0050-3
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TO: Badrul Chowdhury, MD
Director, Division of Pulmonary and Allergy Drug Products
HFD-570

THROUGH: Ladan Jafari
Project Manager
HFD-570

PRODUCT NAME:
Aerospan™
(Flunisolide Hemihydrate, HFA Inhalation Aerosol)

NDA SPONSOR: Forest Pharmaceuticals, Inc.

NDA#: 21-247

SAFETY EVALUATOR: Felicia Duffy, RN

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Aerospan™. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name and its associated label and labeling must be re-evaluated. A re-review of the name will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.
2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to minimize potential errors with the use of this product. We would be willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer. Since Forest Laboratories is sponsor for both Aerobid® and Aerospan™, DMETS recommends the sponsor utilize different labeling and packaging to differentiate between the two drug products.
3. DDMAC finds the proprietary name Aerospan™ acceptable from a promotional perspective.

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**Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; PKLN Rm. 6-34
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: February 27, 2004

NDA# 21-247

NAME OF DRUG: Aerospan™
(Flunisolide Hemihydrate, HFA Inhalation Aerosol)

NDA HOLDER: Forest Pharmaceuticals, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Pulmonary and Allergy Drug Products (HFD-570), for a re-review of the proprietary name Aerospan™, regarding potential name confusion with other proprietary or established drug names. The proposed name was found acceptable by DMETS in a review dated May 8, 2003 (ODS consult #01-0050-2). At that time, DMETS provided suggestions for improvement on the labels and labeling. Revised container labels, carton and insert labeling were provided for review and comment.

Forest Pharmaceuticals is the manufacturer for Aerospan and the currently marketed Aerobid. As per a discussion with the Division Project Manager, Aerospan will replace Aerobid once it is approved. Aerospan contains the same active ingredient as Aerobid, without the chlorofluorocarbon (CFC). As noted in a memorandum to the Division dated March 15, 2001, the average particle size of flunisolide hemihydrate in Aerospan is much smaller than the CFC flunisolide hemihydrate suspension formulation in Aerobid. As a result, the respirable fraction is higher than that in the CFC formulation. Thus, a lower total daily dose of Aerospan is needed to achieve the same effect as Aerobid.

PRODUCT INFORMATION

Aerospan™ (Flunisolide Hemihydrate, HFA Inhalation Aerosol) is indicated for the maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients six years of age and older and for patients requiring oral corticosteroid therapy for asthma. Many of those patients may be able to reduce or eliminate their requirements for corticosteroids over time. Aerospan™ is not indicated for the relief of acute bronchospasm. Flunisolide hemihydrate in HFA is a solution formulation that does not contain chlorofluorocarbons (CFCs) as the propellant. Aerospan™ Inhalation Aerosol should be administered by the orally inhaled route in asthmatic patients aged 6 years and older. The recommended adult (12 and older) starting dose is 2 inhalations twice daily and the maximum daily dose should not exceed 4 inhalations twice daily. The recommended initial dose for children (age 6 to 11) is one inhalation twice daily, not to exceed a maximum dose of 2 inhalations twice daily. Higher doses in children have not been studied. Aerospan™ Inhalation Aerosol is supplied as a pressurized aluminum canister with a two piece purple actuator/gray spacer assembly in one box. Each actuation delivers approximately 139 mcg flunisolide hemihydrate to the patient. Aerospan™ will be available in an 8.9 gram (containing 120 inhalations) and a 5.1 gram (containing 60 inhalations) net weight canister.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2}, as well as several FDA databases³ for existing drug names which sound-alike or look-alike to Aerospan to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁴. The Saegis⁵ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Aerospan. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name Aerospan acceptable from a promotional perspective.
2. The Expert Panel did not identify any additional proprietary names that were thought to have the potential for confusion with Aerospan since the initial interview.

B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. The POCA identified Aerosporin and Aerobid which were considered to have significant phonetic or orthographic similarities to Aerospan. These products are listed in table 2 (see page 3), along with the dosage forms available and usual dosage.

¹ MICROMEDEX Integrated Index, 2003, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-04, and the electronic online version of the FDA Orange Book.

⁴ WWW location <http://www.uspto.gov/tmdb/index.html>.

⁵ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

Table 2: Potential Sound-Alike/Look-Alike Names Identified by POCA

Product Name	Established Name	Dosage Form(s)	Usual Adult Dose	Other
Aerospan	Flunisolide Hemihydrate, HFA	Inhalation Aerosol: 139 mcg/actuation	2 inhalations twice daily	
Aerosporin	Polymyxin B Sulfate Powder for Injection: 500,000 units/vial		<p>IV: 15,000-25,000 units/kg body weight/day every 12 hours not to exceed 25,000 units/kg/day.</p> <p>IM: 25,000-30,000 units/kg/day every 4 or 6 hours.</p> <p>Intrathecal: 50,000 units once daily for 3 to 4 days, then 50,000 units once every other day for at least 2 weeks after cultures are negative.</p>	SA/LA
Aerobid	Flunisolide	Inhalation Aerosol: 250 mcg/actuation	2 inhalations twice daily.	SA/LA
<p>*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)</p>				

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Aerospan, the primary concerns related to look-alike and sound-alike confusion with Aerosporin and Aerobid. The POCA tool identified the names Aerosporin and Aerobid as having significant phonetic and orthographic similarity. Upon further review of the names gathered from POCA, the name Aerosporin was not reviewed further due to numerous differentiating product characteristics such as product strength, indication for use, frequency of administration, and route of administration. Additionally, the last record of sales for Aerosporin was in 1997 according to the Saegis Pharma-In-Use database and the product is no longer marketed.

1. SOUND-ALIKE AND/OR LOOK-ALIKE CONCERNS

Aerobid may look and sound similar to Aerospan. Aerobid contains flunisolide and is also indicated for maintenance treatment of asthma as prophylactic therapy. Aerobid and Aerospan may look and sound similar because they contain the same beginning "Aero". However, Aerobid and Aerospan have orthographically and phonetically different endings ("bid" vs. "span"). Aerobid and Aerospan share overlapping indications for use, active ingredients, frequency of administration, dosage form, route of administration, and sponsor. The differences between the two products is that they are different strengths (250 mcg/actuation vs. 139 mcg/actuation), and Aerobid contains chlorofluorocarbons whereas Aerospan does not. Although the names and product characteristics are similar, DMETS believes that the potential for harm is minimal since the products contain the same ingredient and dosing regimen. In addition, the potential for confusion between the two products should be further minimized since the sponsor will stop marketing Aerobid once Aerospan is approved.

Aerobid

Aerobid

Aerospan

Aerospan

2. OTHER SAFETY CONCERNS

Since Forest Pharmaceuticals is the sponsor for both Aerobid and Aerospan, DMETS recommends the sponsor utilize different labeling and packaging to differentiate between the two drug products. DMETS believes that the aforementioned differentiating orthographic and phonetic characteristics, along with distinct labeling and packaging will help reduce the potential for medication errors between Aerospan and Aerobid during the time Aerobid is co-marketed with Aerospan.

III LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of Aerospan, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified several areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. Please define the value (x) listed where it reads: "*Each actuation of the inhaler delivers 139 mcg of flunisolide hemihydrate*; _____," Revise accordingly on all labels and labeling.
2. Add the _____ flunisolide located in line 40 to the carton labeling to read: "*Each actuation of the inhaler delivers 139 mcg of flunisolide hemihydrate* _____,"
3. Delete trailing zeros throughout the package insert. For example, line 134 states, "*Administration of flunisolide hemihydrate 2.0 mg twice daily....*" The dosage should read 2 mg instead of 2.0 mg. Another example is on line 427 which reads, "... *1.0 mcg/kg/day....*" The dose should read as 1 mcg/kg/day.

B. INSERT LABELING

1. PRECAUTIONS

Information for Patients

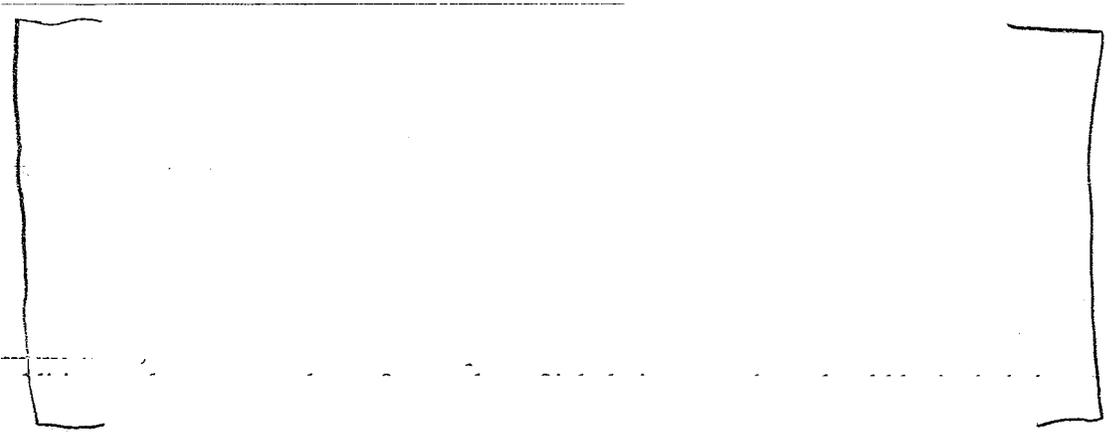
- a. Line 406 states, "*AEROSPAN (flunisolide HFA) Inhalation Aerosol canister contains 120 actuations.*" Since Aerospan is available in different canister sizes, (8.9 grams and 5.1 grams), the statement should list the number of actuations for each canister size.

2. DOSAGE AND ADMINISTRATION

Transferring Patients from Other Inhaled Steroids to AEROSPAN (flunisolide hemihydrate in HFA) Inhalation Aerosol:

- a. Line 601 contains a _____

b.



- c. Line 603 to 605 describes clinical trials performed in children ages 4-11 who successfully transferred from flunisolide CFC to flunisolide HFA. Since Aerospan is indicated to treat children older than 6 years of age, this contradicts the recommended age group of children and may cause confusion. Please comment.

3. PATIENT'S INSTRUCTION FOR USE

- a. Line 679 currently reads, *"Before using new AEROSPAN...."* Revise line 679 to read, *"Before using a new AEROSPAN...."* to avoid misunderstanding of the word "new".
- b. Line 715 states, *"Check that the canister is fully seated in the actuator."* To enhance clarity, please revise the sentence to read as follows, *"Check that the canister is completely inserted into the actuator."*
- c. Clarify the picture in Figure 1 by labeling the canister, mouthpiece and actuator.
- d. Line 761 reads *"...across the back of the purple — ,"* however, it should read *"...purple actuator,"* as indicated throughout the insert.
- e. Bold line 772 and 773 which states, ***"If you are using the inhaler for the first time, or if the inhaler has not been used for more than 2 weeks, you will need to prime (prepare) the inhaler."***
- f. In Figure 11, delete the downward arrow shown. It indicates depressing the actuator, when the figure demonstrates placing the actuator in the mouth.

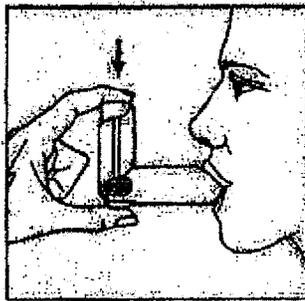


Figure 11

- g. Bold and highlight the word “Caution” in line 806.
- h. In Figure 12, add a downward arrow to accentuate depressing the actuator.

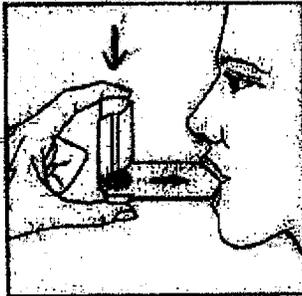


Figure 12

- i. Bold line 823 which states “...rinse your mouth thoroughly with water”
- j. Line 830 bold, highlight and capitalize the words “do not” to read as follows, “...but DO NOT stop using your inhaler...”
- k. Bold line 855 with states, “*If you are using the inhaler for the first time, you will need to prime (prepare) the inhaler.*”
- l. Line 856 instructs the patient to refer to “Step Two” of the package insert. The steps have been deleted from the insert. Please revise accordingly.
- m. Revise lines 859 to 861 to follow as the fourth bullet after line 857.
- n. Revise lines 873 to 875 to follow as the fourth bullet after line 871.

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IV. RECOMMENDATIONS:

- A. DMETS has no objections to the use of the proprietary name Aerospan. DMETS considers this a final review. However, if approval of the application is delayed beyond 90 days, then the name and its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from the signature date of this document.
- B. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review that might lead to safer use of the product. We would be willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer. Since Forest Pharmaceuticals is the sponsor for both Aerobid and Aerospan, DMETS recommends the sponsor utilize different labeling and packaging to differentiate between the two drug products.
- C. DDMAC finds the proprietary name Aerospan acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-3242.

Felicia Duffy, RN
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Alina Mahmud, RPh
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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this page is the manifestation of the electronic signature.**

/s/

Felicia Duffy
3/31/04 08:18:31 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
3/31/04 08:31:50 AM
DRUG SAFETY OFFICE REVIEWER

Jerry Phillips
3/31/04 09:41:28 AM
DRUG SAFETY OFFICE REVIEWER

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CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)**

DATE RECEIVED: March 3, 2003

DUE DATE: July 2, 2003

ODS CONSULT #: 01-0050-2

TO: Badrul Chowdhury, M.D.
Director, Division of Pulmonary and Allergy Drug Products
HFD-570

THROUGH: Ladan Jafari
Project Manager
HFD-570

PRODUCT NAME:
Aerospan
(Flunisolide Hemihydrate, HFA Inhalation
Aerosol)

Manufacturer: Forest Laboratories, Inc.

NDA: 21-247

SAFETY EVALUATOR: Linda Y. Kim-Jung, R.Ph.

SUMMARY: In response to a consult from the Division of Pulmonary and Allergy Drug Products (HFD-570), the Division of Medication Errors and Technical Support (DMETS) conducted a final review of the proposed proprietary name, Aerospan, to determine the potential for confusion with approved proprietary and established names as well as pending names.

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Aerospan. DMETS considers this a final review. However, if approval of the application is delayed beyond 90 days then the name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.
2. DMETS recommends implementation of the labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name, Aerospan, acceptable from a promotional perspective.

Carol Holquist, RPh
Deputy Director,
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242

Fax: (301) 443-9664

Jerry Phillips, RPh
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

**Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; PKLN Rm. 6-34
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: May 8, 2003

NDA#: 21-247

NAME OF DRUG: Aerospan
(Flunisolide Hemihydrate, HFA Inhalation Aerosol)

NDA HOLDER: Forest Laboratories, Inc.

I. INTRODUCTION:

This consult was written in response to request from the Division of Pulmonary and Allergy Drug Products (HFD-570), for assessment of the proprietary name, Aerospan, regarding potential name confusion with other proprietary and established drug names. Additionally, the container labels, carton and insert labeling were provided for review and comment.

In consult 01-0050, dated June 7, 2001, DMETS found the proprietary name "Aerospan" acceptable. However, container labels, carton and insert labeling were not submitted for review at that time.

PRODUCT INFORMATION

Aerospan (Flunisolide Hemihydrate, HFA Inhalation Aerosol) is indicated for the maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients six years of age and older and for patients requiring oral corticosteroid therapy for asthma. Many of those patients may be able to reduce or eliminate their requirements for corticosteroids over time. Aerospan is not indicated for the relief of acute bronchospasm. Flunisolide hemihydrate in HFA is a solution formulation that does not contain chlorofluorocarbons (CFCs) as the propellant. Aerospan Inhalation Aerosol should be administered by the orally inhaled route in asthmatic patients aged 6 years and older. The recommended adult (12 and older) starting dose is 2 inhalations twice daily and the maximum daily dose should not exceed 4 inhalations twice daily. The recommended initial dose for children (age 6 to 11) is one inhalation twice daily, not to exceed a maximum dose of 2 inhalations twice daily. Higher doses in children have not been studied. Aerospan Inhalation Aerosol is supplied as a pressurized aluminum canister with a two piece purple actuator/gray spacer assembly in one box. Each actuation delivers approximately 85 mcg flunisolide hemihydrate (equivalent to 83 mcg flunisolide) to the patient. A — grams (containing 120 inhalations) and — grams (containing 60 inhalations) net weight canister will be available.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2,3} as well as several FDA databases⁴ for existing drug names which sound-alike or look-alike to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁵. An expert panel discussion was conducted to review all findings from the searches. In the initial review (ODS Consult # 01-0050), DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name. The prescription studies were not repeated for this review.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Aerospan. Potential concerns regarding drug marketing and promotion related to the proposed names were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. Since the initial review on June 7, 2001, the Expert Panel identified two additional product names as having the potential for confusion with Aerospan. These names include _____ and Hespan. The new drug application (NDA) for _____ was withdrawn on _____. Therefore, _____ will not be discussed in this review. See Table 1 (see page 4) for available dosage forms and usual dosage of Hespan.
2. DDMAC did not have concerns with the name, Aerospan, with regard to promotional claims.

¹ MICROMEDEX Integrated Index, 2003, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, 2003, Facts and Comparisons, St. Louis, MO.

³ The Drug Product Reference File [DPR], the DMETS database of proprietary name consultation requests, New Drug Approvals 98-03, and the electronic online version of the FDA Orange Book.

⁴ WWW location <http://www.uspto.gov/main/trademarks.htm>

⁵ Data provided by Thomson & Thomson's SAEGIS(tm) Online Service, available at www.thomson-thomson.com.

Table 1 Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel			
Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Aerospan	Flunisolide HFA Inhaler System	Adults and children >12: 2 inhalations twice daily Children (— to 11): 1 — inhalations twice daily	N/A
Hespan	Hetastarch Injection 250 mL and 500 mL IV bags and 500 mL IV bottles	Dosage and infusion rate depends on amount of fluid loss and must be individualized. Adults: Initially, 30-60 g (500-1000 mL) IV infusion. Do not exceed 1.2 g/kg (20 mL/kg) or 90 g (1500 mL) per day. A rate up to 1.2 g/kg/hour (20 mL/kg/hour) may be used in acute hemorrhagic shock. A slower rate is used in septic shock or burns.	L/A
* Frequently used, not all-inclusive. ** L/A (look-alike), S/A (sound-alike)			

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Aerospan, the primary concern raised was related to a look-alike name that currently exists in the U.S. market, Hespan.

The proposed name, Aerospan, may look similar to Hespan depending upon how they are scripted. Hespan injection is used intravenously as a colloidal plasma volume expander to treat hypovolemia and leukapheresis in emergency situations when whole blood or blood products are not available. The dosage and infusion rate depends on the amount of fluid loss and must be individualized. Hespan is supplied as Hespan 6% 500 mL bottles and Hespan 6% 250 mL and 500 mL bags. Hespan and Aerospan share the same letters (E in the first syllable and S, P, A, N in the second syllable) which increases the look-alike potential. Additionally, the letter 'A' can look like the letter 'H' when scripted. However, Aerospan and Hespan differ in indication of use, dosage form (metered dose inhaler vs. injectable) and route of administration (oral inhalation vs. intravenous). Moreover, the setting of use for these two products is different. Hespan is administered by a health care professional in a hospital or a clinic setting in cases of emergency, whereas Aerospan is self-administered by the patient. Also, a prescription for Hespan will require a total volume to be infused and a rate of infusion. Based on the differences between Aerospan and Hespan, the potential for name confusion is minimal.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of Aerospan (February 3, 2003 version), DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified several areas of possible improvement, which might minimize potential user error.

A. GENERAL

1. Increase the prominence of the established name so that it is at least half as large as the letters comprising the proprietary name in accordance with 21 CFR 201.10(g)(2).
2. The terminology: inhalations, actuations, activations, and puffs are used interchangeably throughout the container label, carton and insert labeling. To minimize potential confusion, a single term should be used consistently throughout the literature. See line 541, 545, 546, and 830 for examples.
3. The usual dosage stated on the container label and carton labeling differs from the package insert labeling. The container label and carton labeling state that the usual dose is "one _____ inhalations twice daily, _____." However, the specifics of the _____ are not stated under the Dosage and Administration for either adults (line 541-543) or children (line 545-547). The usual dose including any specifics (e.g., _____) should be the same throughout the product's labels and labeling.

B. CONTAINER LABEL

1. See comments A-1 to A-3.
2. Decrease the prominence of the net quantity statement or increase the prominence of the number of total metered inhalations.
3. The strength is stated in small fine print towards the middle of the side panel. Increase the prominence of the strength to give better visibility and also indicate the equivalent flunisolide dosage per activation [(e.g., Each activation delivers 85 mcg flunisolide hemihydrate (equivalent to 83 mcg flunisolide))].

C. CARTON LABELING

1. See comments A-1 to A-3 and B-2.
2. The strength is stated in small fine print towards the bottom of the main display panel. Increase the prominence of the strength to give better visibility and also indicate the equivalent flunisolide dosage per activation [e.g., Each activation delivers 85 mcg flunisolide hemihydrate (equivalent to 83 mcg flunisolide)].

D. INSERT LABELING

1. See comments A-2 to A-3.

2. PRECAUTIONS

Information for Patients:

- a. Line 361 states, "Aerospan (flunisolide hemihydrate in HFA) Inhalation Aerosol canister contains 120 actuations." Since Aerospan is available in different canister sizes (— grams and — grams), the statement should list the number of actuations for each canister size.
- b. Line 371 states, "Using an in-vitro method at a fixed volume of 2L, each _____ of the label claim) at _____ of the label claim) at 60L/min." This information would be difficult for patients to understand and is mainly targeted towards clinicians. Thus, relocating it to another section (e.g., Clinical Pharmacology) may be more appropriate. Please comment.

3. DOSAGE AND ADMINISTRATION

Transferring Patients from Other Inhaled Steroids to AEROSPAN (flunisolide hemihydrate in HFA) Inhalation Aerosol:

- a. Line 557 contains a _____
[]
- b. []
- c. Line 553 to 555 states, " _____"
[]

- []
- d. Line 559 to 561 describes clinical trials performed in children ages 4-11 who successfully transferred from flunisolide CFC to flunisolide HFA. Since Aerospan is indicated to treat children older than 6 years of age, this contradicts the recommended age group of children and may cause confusion. This information appears to be more appropriate under CLINICAL TRIALS, subsection Pediatric Patients with Asthma. Please comment.

4. PATIENT'S INSTRUCTION FOR USE

- a. Line 624 and 632 makes references to Aerospan being a new product. The word, — should be deleted. We recommend that DDMAC review line 624 to 632 for possible promotional concerns.
- b. Line 735 to 738 states "*If you are using the inhaler for the first time, or if the inhaler has been used for more than 2 weeks, you will need to prime (prepare) the inhaler.*" Highlight the priming instruction.
- c. Bold line 744 which states "*Shake the inhaler immediately before each use.*"
- d. How to Check The contents of Your Canister:

Line 830 states, "*Aerospan (flunisolide hemihydrate in HFA) Inhalation Aerosol contains 120 actuations. Before you reach the final number of actuations, you should contact your doctor to find out if you need a refill.*" Since the product is available in two different sizes (— grams and ~ grams), the statement needs to clarify how many actuations are contained in each canister size. Additionally, the patients should be instructed to keep track of number of inhalations used so that they know when the canister runs out.

IV. RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name Aerospan. DMETS considers this a final review. However, if approval of the application is delayed beyond 90 days then the name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.
2. DMETS recommends implementation of the labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.
3. DDMAC finds proprietary name, Aerospan, acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-3242.

Linda Y. Kim-Jung, R.Ph.
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Denise P. Toyer, Pharm.D.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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/s/

Linda Kim-Jung
7/3/03 09:06:15 AM
PHARMACIST

Denise Toyer
7/3/03 02:28:37 PM
PHARMACIST

Carol Holquist
7/7/03 07:38:23 AM
PHARMACIST

Jerry Phillips
7/7/03 09:09:47 AM
DIRECTOR

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Memorandum

Date: March 15, 2001

To: Robert J. Meyer, M.D.
Director, Division of Pulmonary Drug Products, HFD-570

Through: Sandy Barnes
Project Manager, Division of Pulmonary Drug Products, HFD-570

From: Jerry Phillips, R.Ph.
Associate Director, Office of Post-Marketing Drug Risk Assessment (OPDRA), HFD-400

Subject: OPDRA Consult 01-0050, Aerospan (NDA 21-247)

Reference is made to your January 22, 2001, request for OPDRA to review the proposed proprietary name, Aerospan, for Flunisolide HFA Inhaler System. Flunisolide HFA is a solution formulation that does not contain chlorofluorocarbons (CFCs). The solution formulation in conjunction with a built-in spacer delivers _____ particle size. The average particle size of flunisolide hemihydrate in the new formulation is much _____ than the CFC flunisolide hemihydrate suspension formulation (Aerobid and Aerobid-M), and as a result the respirable fraction is higher than that in the CFC formulation. Therefore, a lower total daily dose of the Flunisolide HFA Inhaler System is required to achieve an equivalent therapeutic effect of the Flunisolide CFC Inhaler System (Aerobid). Despite these differences in particle size and dosing the active ingredient (flunisolide) remains the same between both inhaler systems.

Pursuant to a December 1, 2000, CDER policy meeting with the Center Director, Janet Woodcock, M.D. and senior management, OPDRA will no longer recommend approval of different proprietary names by the same applicant or manufacturer for products that are essentially identical unless there is a compelling reason. The Agency is concerned that the proliferation of proprietary names may be misleading and may also lead to product confusion resulting in medication errors and/or patient harm for the following reasons:

Safety Concerns:

- *Overdose:* Practitioners may become confused and not understand that the two products (Aerobid and Aerospan) contain identical active ingredients. This may increase the risk of a patient being prescribed the same drug product by different physicians, resulting in overuse and/or overdose.
- *Medication errors:* The creation of a new proprietary name for a new formulation of an essentially identical drug product adds unnecessarily to the growing number of proprietary names in the United States. This proliferation of numerous proprietary names

may increase the likelihood of occurrence of medication errors resulting in patient injury due to sound-alike and/or look-alike confusion between products.

Other Concerns:

- *False Inference*: The separate proprietary name infers that there is a unique efficacy that is deserving of a separate name, when in fact this is not true.
- *Management of ADE*: The increasing complexity to manage (regulatory) reports of adverse drug events associated with one active ingredient with 2 or more proprietary names from the same manufacturer.

We believe there are no public health risks or stigmas associated with the use of this drug product and that the safe use of this product is best managed under one proprietary name. We do recognize the need to differentiate the two formulations. However, this can best be handled with the use of a modifier such as "HFA" rather than the use of a new proprietary name. The use of the modifier "HFA" would be consistent with currently established nomenclature for metered dose aerosol systems whose formulations differ due to the hemihydrate component such as Proventil and Proventil HFA.

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/s/

Carol Holquist
3/19/01 07:49:54 AM
PHARMACIST

Jerry Phillips
3/19/01 07:54:11 AM
DIRECTOR

Martin Himmel
3/19/01 01:16:06 PM
MEDICAL OFFICER

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Memo

To: Robert J. Meyer, M.D.
Director, Division of Pulmonary Drug Products
HFD-570

From: Hye-Joo Kim, Pharm.D.
Safety Evaluator, Division of Medication Errors and Technical Support
HFD-400

Through: Carol Holquist, R.Ph.
Deputy Director, Division of Medication Errors and Technical Support
HFD-400

CC: Sandy Barnes
Project Manager, Division of Pulmonary Drug Products
HFD-570

Date: February 11, 2002

Re: ODS Consult 01-0050-1; Aerospan; NDA 21-247

This memorandum is in response to a January 2, 2002 request from your Division for a re-review of the proprietary name, Aerospan. The proposed proprietary name, Aerospan, was found acceptable by DMETS on June 7, 2001 (ODS Consult# 01-0050). The goal date for this application is June 10, 2002.

OPDRA has not identified any additional proprietary or established names that have the potential for confusion with Aerospan since we conducted our review on June 7, 2001 (ODS Consult# 01-0050), that would render the name objectionable. Therefore, we have no objections to the use of this proprietary name.

We consider this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary/established names from this date forward.

If you have any questions or need clarification, please contact the medication errors project manager, Sammie Beam at 301-827-3242.

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this page is the manifestation of the electronic signature.**

/s/

Hye-Joo Kim
2/13/02 09:29:21 AM
PHARMACIST

Carol Holquist
2/14/02 03:15:03 PM
PHARMACIST

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CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: February 23, 2001

DUE DATE:
June 20, 2001

OPDRA CONSULT #: 01-0050

TO: Robert J. Meyer, MD
Director, Division of Pulmonary Drug Products
HFD-570

THROUGH: Sandy Barnes, Project Manager
HFD-570

PRODUCT NAME:

Aerospan (*primary*) _____
(Flunisolide HFA Inhaler System)

Manufacturer: Forrest Laboratories, Inc.

NDA #: 21-247

SAFETY EVALUATOR: Alina R. Mahmud, RPh.

SUMMARY: In response to a consult from the Division of Pulmonary Drug Products (HFD-570), OPDRA conducted a review of the proposed proprietary names "Aerospan" _____ to determine the potential for confusion with approved proprietary and generic names as well as pending names.

OPDRA RECOMMENDATION: OPDRA does not object to the use of the proposed proprietary name "Aerospan".

- OPDRA considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDA's from this date forward.

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3246
Fax: (301) 480-8173

Martin Himmel, M.D.
Deputy Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm. 15B03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: June 7, 2001
NDA NUMBER: 21-247
NAME OF DRUG: Aerospan (primary) or _____
(Flunisolide HFA Inhaler System)
NDA HOLDER: Forrest Laboratories, Inc.

I. INTRODUCTION

This consult was written in response to a request from the Division of Pulmonary Drug Products (HFD-570), for assessment of the tradenames "Aerospan" (primary) _____ (alternate), regarding potential name confusion with other proprietary/generic drug names.

An initial review was conducted on March 15, 2001, where OPDRA recommended that the sponsor utilize the approved proprietary name "Aerobid" for NDA 21-247. However, the review division requested that OPDRA reconsider the proposed names "Aerospan" and _____ because the applicant holder, Forrest Labs, does not own proprietary rights to the name. Furthermore, the division recommended against the use of the dosing schedule "BID" in the name "Aerobid".

PRODUCT INFORMATION

Aerospan and _____ are the proposed proprietary names for Flunisolide HFA Inhaler System and are indicated for the treatment of asthma as prophylactic therapy in adult and pediatric patients four years of age and older. Flunisolide HFA Inhaler System is also indicated for patients requiring oral corticosteroid therapy for asthma. Flunisolide HFA is a solution formulation that does not contain chlorofluorocarbons (CFCs). The solution formulation in conjunction with a built-in spacer delivers _____ particle size. Flunisolide HFA Inhaler System should be administered by the orally inhaled route in asthmatic patients aged 4 years and older. The recommended starting dose for adults 12 years and older is 2 inhalations twice daily. The maximum daily dose should not exceed 4 inhalations twice daily. The recommended dose for children between the ages of 4 and 11 is 1 _____ inhalations twice daily. Flunisolide HFA Inhaler System is supplied as a pressurized aluminum canister with a two piece actuator/spacer assembly in one box. Each actuation delivers 139 mcg of flunisolide hemihydrate from the valve and 85 mcg of flunisolide hemihydrate from the mouthpiece. A _____ g and _____ g net weight canister will be available.

II. RISK ASSESSMENT

The medication error staff of OPDRA conducted a search of several standard published drug product reference texts^{i,ii,iii} as well as several FDA databases^{iv} for existing drug names which sound-alike or look-alike to “Aerospan” to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office’s Text and Image Database was also conducted^v. An Expert Panel discussion was conducted to review all findings from the searches. In addition, OPDRA conducted three prescription analysis studies for each name, to simulate the prescription ordering process.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by OPDRA to gather professional opinions on the safety of the proprietary name “Aerospan”. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of OPDRA Medication Errors Prevention Staff and representation from the Division of Drug Marketing and Advertising Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

Five product names were identified in the Expert Panel Discussion that were thought to have potential for confusion with “Aerospan”. These products are listed in Table 1, along with the dosage forms available and usual FDA-approved dosage.

DDMAC did not have any concerns with the name in regard to promotional claims.

TABLE 1

Product Name	Dosage form(s), Generic name	Usual adult dose	Other**
Aerospan	Alimskolide HFA Inhaler System	Adults: 2 inhalations twice daily Children (age 4 to 10): 1 inhalation twice daily	
Aerozoin	Tincture of Benzoin 30%, Isopropyl alcohol 44.8% Spray	Use as directed	S/A, L/A per OPDRA
Aricept	Donepezil HCl 5 mg and 10 mg tablets (Rx)	5 to 10 mg once daily	S/A, L/A per OPDRA

ⁱ MICROMEDEX Healthcare Intranet Series, 2000, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician’s Desk Reference (Medical Economics Co. Inc, 2000).

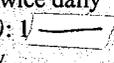
ⁱⁱ American Drug index, 42nd Edition, 1999, Facts and Comparisons, St. Louis, MO.

ⁱⁱⁱ Facts and Comparisons, 2000, Facts and Comparisons, St. Louis, MO.

^{iv} COMIS, The Established Evaluation System [EES], the Labeling and Nomenclature Committee [LNC] database of Proprietary name consultation requests, New Drug Approvals 98-00, and online version of the FDA Orange Book.

^v WWW location <http://www.uspto.gov/tmdb/index.html>.



Product Name	Dosage form(s), Generic name	Usual adult dose*	Other**
Aerospan	Flunisolide HFA Inhaler System	Adults: 2 inhalations twice daily Children (age 4 to 11): 1  inhalations twice daily	
Irospan	Ferrous sulfate 65 mg with Ascorbic Acid tablets and capsules (otc)	1 tablet or capsule once daily or as directed by physician	S/A, L/A per OPDRA
Aristospan	Triamcinolone hexacetonide 5mg/mL intralesional injection and 20 mg/mL intra-articular injection (Rx)	Intra-articular: 2 to 20 mg average. Large joints (eg, knee, hip, shoulder)- 10 to 20 mg. Small joints (eg, interphalangeal, metacarpophalangeal)- 2 to 6 mg. Intralesional or sublesional: Up to 0.5 mg per square inch of affected area.	S/A, L/A per OPDRA
Histospan	Chlorpheniramine maleate; phenylephrine hydrochloride; hysocine methonitrate	No longer marketed	
		*Frequently used, not all-inclusive.	**L/A (look-alike), S/A (sound-alike)

B. STUDY CONDUCTED BY OPDRA

1. Methodology

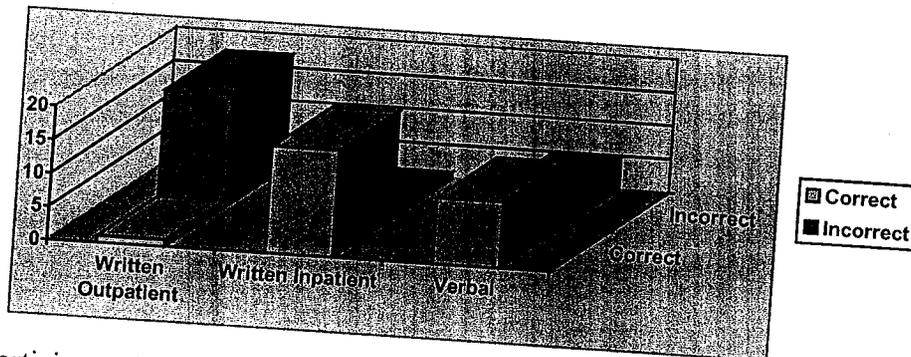
A separate study was conducted within FDA for the proposed proprietary name to determine the degree of confusion of “Aerospan” with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 86 health care professionals (nurses, pharmacists, and physicians). This exercise was conducted in an attempt to simulate the prescription ordering process. An OPDRA staff member wrote an inpatient order and outpatient prescriptions, each consisting of a combination of marketed and unapproved drug products and prescriptions for “Aerospan” (see below). These written prescriptions were optically scanned and one prescription was delivered via email to each study participant. In addition, one OPDRA staff member recorded a verbal outpatient prescription that was then delivered to a group of study participants via telephone voicemail. Each reviewer was then requested to provide an interpretation of the prescription via email.

HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
Outpatient: Aerospan # 1 Sig: 2 puffs BID	Aerospan inhaler 2 puffs twice daily Dispense #1 unit
Inpatient: Aerospan 2 puffs BID #1	

2. Results

Results of these exercises are summarized below:

Study	No. of participants	# of responses (%)	"Aerospan" response	Other response
Written: Outpatient	28	18 (64%)	1 (6%)	17 (94%)
Inpatient	30	17 (57%)	16 (94%)	1 (6%)
Verbal	27	15 (56%)	10 (67%)	5 (33%)
Total:	85	50 (59%)	27 (54%)	23 (46%)



Among participants in the two written prescription studies, 18 of 35 respondents (51%) interpreted the name incorrectly. The interpretations were misspelled variations of "Aerospan" such as *Aerospar* and *Aerosporan*. Other interpretations included *Serispan*, *Duraspar* and *Derospar*.

Among verbal prescription study participants, 5 out of 15 study participants (33%) interpreted the name incorrectly. Most of the incorrect name interpretations were phonetic variations of "Aerospan" such as *Arospan*, *Araspan*, and *Arispan*.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name "Aerospan", the primary concerns raised were related to a couple sound-alike, look-alike names that already exist in the U.S. marketplace. Two products, Aricept and Irospan, were believed to be the most problematic in terms of potential medication errors.

OPDRA conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that Aerospan could be confused with Aricept or Irospan. Negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to small sample size. The majority of the incorrect responses from the verbal and written prescription studies were misspelled/phonetic variations of the drug name and did not overlap with a currently marketed drug product.

Aricept is the proprietary name for donepezil hydrochloride and is indicated for the treatment of mild to moderate dementia of the Alzheimer's type. Aricept is available as a 5 mg and 10 mg tablet. The dosages of Aricept shown to be effective are 5 mg and 10 mg administered once per day. Although Aerospan and Aricept do not look similar when scripted, the names sound somewhat similar. However, Aerospan and Aricept differ in dosage form, dosing frequency and strength. Given the above differences in combination with the lack of convincing look-alike and sound-alike potential, there is insufficient evidence at this time to conclude that the proposed drug name would be confused with Aricept.

Irospan is the proprietary name for an over-the-counter ferrous sulfate preparation. Each tablet and capsule of Irospan contain 65 mg of ferrous sulfate. Irospan is indicated for the treatment of iron deficiency and iron deficiency anemia. The recommended dose of Irospan is one tablet or capsule once daily. Aerospan and Irospan not only look similar when scripted, the drug names sound similar as well. Although Irospan is available as an over-the-counter drug product, a written prescription may be presented to the pharmacist for insurance reimbursement purposes. In addition, healthcare practitioners often omit the strength on a prescription when a drug product is available in only one strength. This will be the case for Aerospan and Irospan, as each is available in one strength therefore increasing the risk of confusion between the two drug products. However, Aerospan and Irospan differ in dosing schedule and dosage form. Therefore, OPDRA believes that the risk of confusion associated with these two drugs is relatively low.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

We have no comments.

IV. RECOMMENDATIONS

OPDRA does not object to the use of the proposed proprietary name "Aerospan".

OPDRA would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam, R.Ph. at 301-827-3231.

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