CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-592

PROPRIETARY NAME REVIEW(S)

MEMORANDUM	Division of Medication Errors and Technical Support Office of Surveillance and Epidemiology WO 22, Mailstop 4447, HFD-420 Center for Drug Evaluation and Research

To: Badrul Chowdhury, MD
Director, Division of Pulmonary and Allergy Products
HFD-570

Through: Linda Kim-Jung, PharmD, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support, HFD-420

From: Kristina C. Arnwine, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

Date: August 10, 2006

Subject: OSE Review 03-0011-5 Foradil Certihaler (Formoterol Fumarate Inhalation Powder) 8.5 mcg/actuation; NDA 21-592

This memorandum is in response to a July 17, 2006 request from your Division for a re-review of the proprietary name Foradil Certihaler. The package insert and medication guide were included for review and comment. Neither a sample device or revised container labels and carton labeling were submitted for review at this time.

DMETS found the name Foradil Certihaler acceptable in ODS Consult 03-0011 (dated May 7, 2003) and in ODS Consult 03-0011-1 (dated December 1, 2004). Additionally, DMETS reviewed the Patients Instructions for Use and Educational Campaign in two subsequent reviews dated February 3, 2005 (ODS Consults 03-0011-2 and 03-0011-3) and January 31, 2006 (ODS Consult 03-0011-4).

Since the initial review of Foradil Certihaler, DMETS has not identified any additional names that have the potential for look-alike and/or sound-alike confusion with Foradil Certihaler.

In ODS Consult 02-0118 dated December 23, 2004, DMETS previously reported errors associated with the use of Foradil. The medication errors were related to oral ingestion of the capsules for inhalation (n=30), product failures (n=4), proprietary name confusion with Toradol® (n=3), expiration dating and storage confusion (n=2), and look-alike confusion between the active Foradil® capsules and the placebo capsules used for training purposes (n=1). There were also reports of confusion with the storage and expiration dating used with Foradil® Aerolizer®. The reports were received by the Agency between June 2001 and September 2004.

For this review, DMETS conducted a search of the Adverse Event Reporting System (AERS) to determine if there were any additional medication errors associated with use of Foradil since the previous AERS search that might be relevant to the labels and labeling of this product.

The search identified eleven additional medication error cases (n=11) associated with the use of Foradil. Two (n=2) of the eleven cases were foreign reports (Germany) that pertained specifically to Foradil Certihaler. In both cases, the device malfunctioned, delivering the entire contents of the device in a single dose. The remaining nine cases (n=9) involved the use of Foradil Aerolizer. The errors included oral administration of the capsules for inhalation (n=7), product failure (n=1), and wrong technique (n=1). The search did not identify any new cases of name confusion between Foradil and Toradol or any other drug products. See attachment A for a complete listing of all eleven cases.

Although use of the "Certihaler" should eliminate errors associated with oral administration of the Foradil capsules used in the Aerolizer, DMETS is concerned about the potential for overdoses as a result of device malfunction as identified in the AERS cases. DMETS recommends ensuring that all precautions are taken to prevent device malfunction and ensure overdoses of Foradil do not result from proper use of the Certihaler. Additionally, DMETS refers to ODS Consult 03-0011-2 and 03-0011-4, which contained comments concerning the Certihaler device.

DMETS also provides the following additional labeling comments or areas of improvement, which should minimize potential user error.

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Attachment A

FDA Receipt Date AERS #	Type of Error	Narrative
		Wrong Route of Administration
04/14/2005 4634911-9	Wrong Route	A 9 year-old female patient accidentally swallowed a Foradil (formoterol fumarate) capsule on 02 Mar 2004. It was the patient's first dose. No further information was provided. The patient's mother stated "the inhaler device did not work properly and my daughter swallowed the pill. We discontinued the product. We monitored her. She has been fine."
04/15/2005 4636110-3	Wrong Route	The patient was prescribed Foradil (formoterol fumarate) inhalation capsule for COPD. She took orally one capsule at 11:00 and one capsule at 20:00 on 30 March 2005. That evening she had tremor, nausea and vomiting. She was hospitalized on [redacted] Foradil was discontinued. Symptomatic treatment was given. The patient completely recovered. Foradil treatment was started again. The reaction did not reappear after reintroduction.
06/07/2005 4653911-1	Wrong Route	The patient called in herself to report that she accidentally swallowed a Foradil (formoterol) 12 mcg capsule on 28 May 2005 instead of inhaling it. At the time of the report, she had remained asymptomatic. She has been taking Foradil for chronic bronchitis for approximately 2 years.
09/07/2005 4762389-3	Wrong Route	Patient with a history of diabetes since 2003, hypertension since 2003 and "cholesterol" since 2004, on multiple drug therapy, started treatment with Foradil 12 mcg (formoterol fumarate) in Jul 2004 to treat pulmonary emphysema…On 30 Aug 2005, the patient swallowed one capsule of Foradil by mistake. The patient did not present any reaction.
01/12/2006 4878585-0	Wrong Route	A 75 year-old female patient took 1x2 capsule Spiriva (tiotropium) and 1x7 capsules Foradil (formoterol) accidentally and was hospitalized into an intensive care unit. As symptoms tremor, tachycardia 110 ≤ 120, respiratory insufficiency and confusion were reported. Treatment is unknown. Outcome was reported to be unknown.
02/21/2006 4917048-0	Wrong Route	A patient with a history of pre-existing congestive heart failure was hospitalized for exacerbation of congestive heart failure "for a while" (exact date unknown). The patient came in on Foradil inhaler (formoterol). It was unspecified what dose, indication and how long the patient had been taking Foradil inhaler. On 06 Feb 2006, a nurse mistakenly gave the patient Foradil capsule to take orally with his other drugs instead of inhaling the Foradil powder via the inhaler (aerolizer). The patient was observed with no ill effects.
05/06/2005 4654998-7	Wrong Route	The patient, taking Foradil (formoterol) for an unspecified amount of time, reported that she experience a stomach ache the night before and "has not gone to sleep all night." As a result she accidentally swallowed a Foradil capsule today. She further mentioned that her stomach "has not been right ever since she had gall bladder removed in Oct and was waiting to call her stomach doctor"
		Device Failure
09/02/2005 4759998-4	Product Problem	This patient, who was taking Foradil (formoterol fumarate) for about 2 years, reported that she felt that she may be inhaling a part of the capsules at times (stated "inhaling plastic now and then"). In addition, she stated that her Aerolizers do not always pierce the capsules on the first attempt (noticed with several units in the past) and her asthma "got worse". The patient further stated she had "a lung nodule". No further details were provided. The consumer was advised by a Schering Plough associated that in rare cases, the Foradil capsules may be shattered in to small pieces, which should be retained by screen built into the Aerolizer Inhaler but possibly that rarely, tiny pieces of gelatin capsule might reach user's mouth or throat upon inhalation.
05/05/2006 4994084-4 German report	Product Problem	A patient has been treated wit Foradil Certihaler (formoterol). On 03 Jan 2006, before inhalation, the inhaler's dose-meter showed that there were still 33 puffs available. During inhalation, a large and visible amount of white powder was set free. The patient suspected that the complete content of powder was released from the inhaler. The dose-meter showed 32 remaining doses after the inhalation. In the further course, the patient showed a heart rate at rest of 145/min and a blood pressure of 150/100 mmHg, as well as dizziness and headache. This condition lasted for about one day; the patient was in physician surveillance for a few hours. The outcome was reported as recovered…The devices was forwarded to Quality Assurance for testing…1.01 mg of residual powder was found in the reservoir… The minimal expected powder at the counter display reading 30 was calculated to 290.4 mg. Based on this difference the apparent overdose was confirmed. In a further note, QA confirmed that in the interior of the device, there was a distortion damage due to misuse; this damage can result in powder leakage and could be reproduced by forcibly removing the cap. However this required considerable force and was contrary to the instructions given in the leaflet.

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FDA Receipt Date AERS #	Type of Error	Narrative
05/05/2006 4994083-8	Product Problem	This patient has previously been treated with Foradil P (formoterol dry powder in capsules with aerolizer). He was switched to Foradil Certihaler (formoterol multiple dose dry powder inhaler) about 2 months ago. Following the switch he had used 3 devices of Foradil Certihaler without any problems. In the evening hours of 22 Jan 2006, with the 4th device, at a dose counter position of 43, he opened the device routinely and inhaled. The dose counter position changed to 42. After this inhalation he recognized there was more powder in his mouth and also on his hand. He estimated that the amount inhaled was about 4 times the normal dosage. About 5 to 10 minutes after the inhalation, he started to suffer from shaking of hands and legs, as well as restlessness and chills. He also experienced redness of the head and a heat sensation. His heart rate increased to about 180/min, this was measured several times; there was also an irregular pulse. These conditions lasted until late night of the same day. The outcome was reported as recovered...The device was forwarded to Quality Assurance...The residual amount of powder in the reservoir was found to be 0.07 mg. The minimal expected residue at counter display reading 40 was 354.8 mg. Based on this difference, the apparent overdose was confirmed. In a further note, QA confirmed that in the interior of the device, there was a distortion damage due to misuse; this damage can result in powder leakage and could be reproduced by forcibly removing the cap. However this required considerable force and was contrary to the instructions given in the leaflet.
Wrong Technique		
01/31/2006 4896376-1	Wrong Technique	While preparing a Foradil (formoterol) sample for his patient who was having a severe asthma attack, the physician made a mistake in handling the device, he placed the capsule directly in to the mouthpiece instead of putting it in the Aerolizer Inhaler chamber. There the patient almost choked on the whole capsule while inhaling.

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/s/

Kristina Arnwine
9/20/2006 09:52:36 AM
DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
9/20/2006 09:59:00 AM
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Denise Toyer
9/20/2006 10:38:26 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
9/20/2006 11:36:47 AM
DRUG SAFETY OFFICE REVIEWER

Office of Drug Safety

Memo

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

From: Tia Harper-Velazquez, Pharm.D.
Safety Evaluator, Division of Medication Errors and Technical Support, Office of Drug Safety
HFD-420

Through: Alina Mahmud, R.Ph., Team Leader
Carol Holquist, R.Ph.., Director
Division of Medication Errors and Technical Support, Office of Drug Safety
HFD-420

CC: Akilah Green
Project Manager, Division of Pulmonary and Allergy Drug Products
HFD-570

Date: November 24, 2004

Re: ODS Consult 03-0011-1: Foradil Certihaler (Formoterol Fumarate), Inhalation Powder, 8.5 micrograms/actuation; NDA 21-592

This memorandum is in response to a November 3, 2004, request from your Division for a re-review of the proprietary name, Foradil Certihaler. In our last review, dated April 23, 2003, (ODS Consult # 03-0011), DMETS did not have any objections to the use of the proprietary name Foradil Certihaler. Since that review, DMETS has not identified any additional proprietary or established name as having the potential to cause name confusion with Foradil Certihaler. In addition, DMETS searched the Adverse Event Reporting Systems (AERS) database to identify post-marketing reports of confusion with the currently marketed product Foradil capsules. All reports identified in AERS pertain to the labels and labeling specific to Foradil capsules. These issues will be addressed in a separate consult from DMETS. Therefore, DMETS has no objections to the name.

The carton and package insert labeling were previously submitted for review with the initial consult. From the revised package insert labeling retrieved from the Electronic Document Room, it appears that the sponsor has revised the "Patient Information Materials" section of the package insert per DMETS recommendations. DMETS refers the sponsor to ODS Consult # 03-0311, dated April 21, 2003, for carton labeling comments (Physician sample and stocks supply.)

DMETS 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 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 DMETS' Project Manager, Sammie Beam at 301-827-2102.

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

/s/

Tia Harper-Velazquez
12/1/04 09:13:08 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
12/1/04 12:56:39 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
12/1/04 01:09:18 PM
DRUG SAFETY OFFICE REVIEWER

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

DATE RECEIVED: 11/16/03	**DUE DATE:** 5/5/03	**ODS CONSULT #:** 03-0011

TO:

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

THROUGH:

Craig Ostroff
Project Manager
HFD-570

PRODUCT NAME:	**IND SPONSOR:** Novartis Pharmaceuticals
Foradil Certihaler (Formoterol Fumarate) Inhalation Powder Each actuation delivers 8.5 mcg of Formoterol Fumarate **IND #:** 60,254	

SAFETY EVALUATOR: Alina R. Mahmud, 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 review of the proposed proprietary name "Foradil Certihaler" 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 name Foradil Certihaler. In addition, DMETS recommends that the sponsor commit to providing an educational campaign at the launch of this product in order to minimize confusion that may arise as a result of Foradil Aerolizer and Foradil Certihaler being co-marketed.
2) DDMAC finds Foradil Certihaler acceptable from a promotional perspective.
3) In addition, DMETS recommends implementation of the labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.

This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated upon submission of the NDA and 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 this date forward.

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

PROPRIETARY NAME REVIEW

DATE OF REVIEW: April 21, 2003

IND NUMBER: 60,254

NAME OF DRUG: Foradil Certihaler
(Formoterol Fumarate) Inhalation Powder

IND HOLDER: Novartis Pharmaceuticals

I. INTRODUCTION:

This consult was written in response to a request from the Division of Pulmonary and Allergy Drug Products (HFD-570) for assessment of the tradename "Foradil Certihaler", regarding potential name confusion with other proprietary/established drug names. The draft carton and patient insert labeling were provided for review and comment. The sponsor has submitted additional information, including an independent analysis conducted by the Brand Institute (BI) for review and comment.

The proprietary name "Foradil" has been in the marketplace since February 16, 2001. The currently marketed Foradil Aerolizer consists of a capsule dosage form containing a dry powder formulation of Foradil (formoterol fumarate) intended for oral inhalation only with the Aerolizer™ Inhaler. The indications for use are the same for both dosage forms.

PRODUCT INFORMATION

Foradil Certihaler is a breath-actuated multi-dose dry powder inhaler, which contains a powder formulation of formoterol fumarate intended for oral inhalation only. Each actuation of Foradil Certihaler delivers approximately 8.5 mcg of formoterol fumarate from the mouthpiece, corresponding to a metered dose of 10 mcg of formoterol fumarate. Foradil Certihaler is indicated for long-term, twice-daily (morning and evening) administration in the maintenance treatment of asthma and in the prevention of bronchospasm in adults and children 5 years of age and older, [redacted] b(4)

It is not indicated for patients whose asthma can be managed by occasional use of inhaled, short-acting, beta$_2$-agonists. Each inhaler delivers 60 doses.

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 databases[3] for existing drug names which sound-alike or look-alike to Foradil Certihaler 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[4]. The Saegis[5] 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. In addition, DMETS conducted three prescription analysis studies for each name, 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.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Foradil Certihaler. 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. The Expert Panel discussed the results of a search conducted in FDA Adverse Event Reporting System (AERS). This search discovered two medication error reports between the currently marketed Foradil and the marketed drug product Toradol. The Expert Panel identified five additional proprietary names as having the potential for confusion with "Foradil Certihaler." These products are listed in Table 1 (see page 4), along with the dosage forms available and usual dosage. Additionally, the Expert Panel identified and discussed the potential for confusion with other product names that utilizing "haler" as part of their names. These names included "Spinhaler", "Pockethaler", "Turbihaler", and "Twisthaler".

2. DDMAC did not have concerns about the name, Foradil Certihaler, with regard to promotional claims.

[1] MICROMEDEX Healthcare Intranet Series, 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] The Established Evaluation System [EES], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 00-03, 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(tm) Online Service, available at www.thomson-thomson.com.

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

Product Name	Established name, Dosage form(s)	Usual adult dose*	Other**
Foradil Certihaler	**Formoterol Fumarate Inhalation Powder *Each actuation delivers 8.5 mcg of Formoterol Fumarate**	**One inhalation every 12 hours.**	
Foradil	Formoterol Fumarate Inhalation Powder *Each actuation delivers 10 mcg of Formoterol Fumarate	One inhalation every 12 hours.	Look-alike, Sound-alike
Toradol	Ketorolac Tromethamine Tablets 10 mg Injection: 15 mg/mL and 30 mg/mL	10 mg to 60 mg daily. Daily doses may be divided and given every 4 to 6 hours.	Look-alike
Fiorital	*Aspirin, Caffeine and Butalbital Tablets*	*No longer marketed.*	Look-alike
Fiorinal	Aspirin, Caffeine and Butalbital Tablets 325 mg/30 mg/50 mg	1 to 2 tablets every 4 hours as needed.	Sound-alike
Lorabid	Loracarbef Capsules 200 mg and 400 mg Powder for Oral Suspension: 100 mg/5 mL and 200 mg/5 mL	200 mg to 400 mg once or every 12 hours depending on severity of infection.	Look-alike

*Frequently used, not all-inclusive

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of Foradil Certihaler 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 105 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescriptions for Foradil Certihaler (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via
e-mail to the medication error staff.

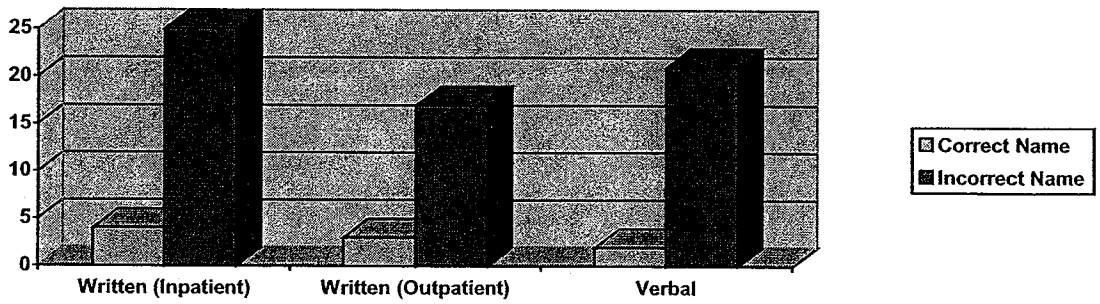
HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: Foradil Cert. Inhaler Sig: 1 puff q12h #1	Foradil Certihaler Dispense #1 Sig: 1 puff every 12 hours
Inpatient RX: Foradil Certihaler 1 puff q12h	

2. Results:

The results for Foradil Certihaler are summarized in Table I.

Table I

Study	# of Participants	# of Responses (%)	Correctly Interpreted (%) "Foradil Certihaler"	Incorrectly Interpreted (%)
Written Inpatient	35	26 (74%)	2 (77%)	24 (23%)
Written Outpatient	31	23 (74%)	15 (65%)	8 (35%)
Verbal	39	27 (69%)	0 (0%)	27 (100%)
Total	105	76 (72%)	17 (22%)	59 (78%)



Among participants in the written prescription studies, 32 of 49 respondents (65%) interpreted the name incorrectly. The interpretations were misspelled variations of "Foradil Certihaler". Responses of "Foradil" without "Certihaler" were scored as incorrect. Incorrect interpretations of the written prescriptions included: *Foradil (3), Foradil Cert Inhaler (2), Foradil Airhaler,*

Foradil Cert Traler, Foradil Cat. Haler, Foradil Artihale (9), Fordil Cortihale, Foradile Artihale (2), Foradil Ceritrate (2), Foradil Certihale (3), Foradil Certihaler (2), Foradil Cortihaler, Foradil Astihale, Foradil Arihale, Foradil haler, and *Floradil.*

Among participants in the verbal prescription studies, 27 of 27 (100%) interpreted the name incorrectly. Most incorrect name interpretations were phonetic variations of "Foradil". Responses of "Foradil" without the "Certihaler" were considered incorrect. Incorrect interpretations of the verbal prescription included: *Foradil (13), Floradil, Foradyl Inhaler, Floradil Thirty-haler, Foradil Thirty-Haler (3), Foradil 30-haler, Foradel, Foridil 30haler, Foradil inhaler, Foridol, Foridil (2),* and *Floridel.*

C. AERS SEARCH

A search was conducted through the FDA Adverse Event Reporting System *(AERS)* database for all post-marketing safety reports of medication errors reported for terms "Foradil%" and "Formoterol%", using the MedDRA Preferred Term, MEDICATION ERROR. The search yielded eleven reports pertaining to the wrong route of administration of Foradil Capsule where the capsule was taken orally rather than inhaled via an aerolizer. These reports will be discussed in a separate post-marketing consult from DMETS. An additional report pertaining to name confusion between Toradil and Foradil was identified. In this case, the medication never reached the patient.

AERS Report #	Date	Narrative
3921204-8	May 20, 2002	Hospital order written for Foradil bid interpreted as Toradol bid. Patient with history of arthritis pain and COPD. Potential medication error caused by look-alike drug names. Caught before medication was administered.

D. SAFETY EVALUATOR RISK ASSESSMENT

1. Look-alike, Sound-alike Names

In reviewing the proposed proprietary name "Foradil Certihaler", the primary concerns raised related to look-alike, sound-alike confusion with names already in the U.S. marketplace. The products considered to have potential for name confusion with Foradil Certihaler were Foradil, Fiorinal, Lorabid and Toradol.

DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that Foradil Certihaler can be confused with Lorabid, Fiorinal, or Toradol. The majority of interpretations from the written and verbal prescription studies were phonetic/misspelled interpretations of the drug name Foradil Certihaler. However, there was confirmation that Foradil Certihaler can be confused with Foradil. Twenty-nine percent of participants in the written study and verbal study did not include "Certihaler" with the root name as they provided "Foradil" as an interpretation.

The Expert Panel expressed concern with the potential for errors with the marketed product Foradil Aerolizer and Foradil Certihaler. Although Foradil and Foradil Certihaler share the same active ingredient, indication, dosing regimen, and similar dose delivered via mouthpiece (8.5 mcg vs. 10 mcg), harm may occur if the patient inadvertently receives Foradil Aerolizer instead of Foradil Certihaler. If the patient correctly uses Foradil Aerolizer, harm will not occur.

However, if the patient ingests the oral capsule rather than administer the dose using an Aerolizer, as was done in the post-marketing error reports for Foradil Aerolizer, the patient may not experience the benefits of the drug since the oral route does not effectively deliver the drug to the lungs.

Fiorinal and Foradil, without the modifier "Certihaler", sound similar. Fiorinal contains aspirin, caffeine and butalbital and is indicated for the treatment of complex tension headaches. Fiorinal and Foradil sound similar because they share the letters "F", "or", "a" and "l". Despite sound-alike similarities, Foradil Certihaler and Fiorinal have differences which make them distinct from each other. These products do not share a common dosage form. Foradil Certihaler is available as an inhaler while Fiorinal is available as tablets. They differ in directions of use (twice daily vs. every 4 hours, as needed) as well. Additionally, no reports of confusion were identified between the marketed product Foradil and Fiorinal. The likelihood of confusion is further minimized with Foradil Certihaler since the modifier Certihaler will likely be used in association with the name.

Lorabid and Foradil, without the modifier, look somewhat similar. Lorabid is an antibiotic structurally related to cephalosporins. Lorabid and Foradil can look similar since the share the letters "ora" and "i". In addition, the letters with an upstroke are positioned in the same order (L vs. F, b vs. d, d vs. l). Despite the name similarities, Lorabid and Foradil differ with respect to other characteristics such as strength and dosage form (10 mcg vs. 200 mg and 400 mg capsules, 100 mg/5 mL and 200 mg/5 mL oral suspension). Although the products share a dosing regimen of every 12 hours, the likelihood of confusion is minimal given that no medication errors have been reported for the currently available Foradil and Lorabid. Additionally, Certihaler will be used in conjunction with the root name Foradil.

Foradil Lorabid

The Expert Panel expressed concern between Foradil Certihaler and Toradol because one error report was identified in a search of the AERS database where a prescription for Foradil was filled as Toradol. The error was caught before the medication was dispensed to the patient. The names look almost identical when scripted if Foradil is scripted without the modifier. Toradol is indicated for the short-term (5 days) management of moderately severe acute pain that requires analgesia at the opioid level, usually in a postoperative setting. The AERS report states that the error was committed because the names look similar (see below). In this case, the dosing interval overlapped (BID).

Foradil Toradol

However, despite look-alike similarities, Toradol and Foradil Certihaler have differences which make them distinct from each other. Toradol is available as a tablet and injection while Foradil Certihaler will be available as an inhaler. The drug products also differ in dosing regimen. Toradol is given every 4 to 6 hours while Foradil Certihaler is given every 12 hours. Additionally, "Certihaler" will be used in conjunction with the root name Foradil which will further distinguish one name from the other. Therefore, DMETS believes that the potential for

confusion between Foradil Certihaler and Toradol is minimal. However, we will continue to monitor post-marketing reports of confusion between these two names.

2. Modifier

We acknowledge that other currently marketed drug products (i.e., Maxair Autohaler and Vancenase Pockethaler) utilize various modifiers for inhalers. Upon review, DMETS determined that the potential for confusion between the proposed modifier "Certihaler" and the existing modifiers is minimal as they lack look-alike and sound-alike potential. Therefore, DMETS has no concerns with the use of the modifier "Certihaler" in Foradil Certihaler. However, we recommend that the labels and labeling of Foradil Aerolizer and Foradil Certihaler appear distinctly different. In addition, we recommend that the sponsor commit to providing an educational campaign at the launch of this product in order to minimize confusion that may arise as a result of Foradil Aerolizer and Foradil Certihaler being co-marketed.

E. [redacted] REVIEW

The sponsor submitted an independent analysis conducted by [redacted] for review and comment. [redacted] conducted research to determine whether there are any safety risks associated with the name Certihaler as a proprietary name candidate for a formoterol fumarate. The following drug names were identified as having a sound-alike and look-alike potential to Foradil Certihaler: Asthmahaler, Ceredase, Ceretex, Certagen, Certa-vite, Cervidil, Cylert, Halercol, Medihaler-iso, Serpalan, Serpasil, Sertabs, and Sertina. A comparison of the product profiles of existing drugs and Certihaler showed little commonality. Overall, the proposed proprietary name Certihaler received a favorable safety evaluation based upon all four sections of [redacted] methodology. b(4)

DMETS concurs with [redacted] findings in that Certihaler has a low potential for confusion with the identified drug names. Therefore, the proposed proprietary name Certihaler is acceptable from a safety perspective.

III. LABELING, PACKAGING AND SAFETY RELATED ISSUES:

In the review of the carton and patient package insert labeling for Foradil Certihaler, DMETS has focused on safety issues relating to possible medication errors and has identified several areas of possible improvement, which might minimize potential user error.

A. CARTON LABELING (Physician sample and stock supply)

1. Please ensure that the labels and labeling for Foradil Aerolizer and Certihaler are distinctly different. In order to differentiate the two products, we recommend utilizing contrasting colors, boxing, or some other means.

2. The font size utilized for the modifier "Certihaler" should be identical to the font size of the root name "Foradil". The current presentation highlights "Foradil" and not "Certihaler". Please revise accordingly.

3. The yellow line stretched above and across the name is distracting and detracts attention away from the proprietary name. Please delete.

B. PATIENT INFORMATION MATERIALS

1. The pictorials on pages 3 and 4 are not numbered while the pictorials on the subsequent pages are numbered with each step. We recommend that the pictorials on page 3 and 4 be numbered as well.
2. [redacted]

b(4)

4.

5.

APPEARS THIS WAY
ON ORIGINAL

IV. RECOMMENDATIONS:

A. DMETS has no objections to the use of the name Foradil Certihaler. In addition, we recommend that the sponsor commit to providing an educational campaign at the launch of this product in order to minimize confusion that may arise as a result of Foradil Aerolizer and Foradil Certihaler being co-marketed.

B. DDMAC finds the name, Foradil Certihaler, acceptable from a promotional perspective.

C. DMETS recommends the labeling revisions as outlined in Section III of this review that might lead to safer use of the product. We would be willing to revisit these issues when the Division receives a revised draft of the labeling from the manufacturer.

This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated upon submission of the NDA and 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 this date forward.

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.

Alina R. Mahmud, R.Ph.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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/s/

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