CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-124s000

OTHER REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	November 19, 2007
To:	Badrul Chowdhury, MD, Director Division of Pulmonary and Allergy Products
Thru:	Linda Kim-Jung, PharmD, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Errors and Technical Support
From:	Kristina C. Arnwine, PharmD, Safety Evaluator Division of Medication Errors and Technical Support
Subject:	DMETS Label and Labeling Review
Drug Name(s):	Omnaris (Ciclesonide Nasal Spray)
Application Type/Number:	NDA#: 22-124
Submission Number:	N/A
Applicant/sponsor:	Altana Pharma
OSE RCM #:	2007-1985

1 BACKGROUND

1.1 INTRODUCTION

This memorandum is in response to a September 17, 2007 request from the Division of Pulmonary and Allergy Products for a review of the Patient's Instructions for Use and package insert labeling for Omnaris.

1.2 REGULATORY HISTORY

Omnaris was approved by the Agency on October 20, 2006 for use in patients 12 years of age and older. (b) (4) The sponsor submitted a response to the approvable letter for use in pediatric patients on May 24, 2007.

1.3 PRODUCT LABELING

Omnaris is a glucocorticoid indicated for the treatment of nasal symptoms associated with seasonal and perennial allergic rhinitis in adults and adolescents (b) (4). The usual dose is two sprays in each nostril once daily for adults and children six years of age and older. (b) (4). The usual dose is two sprays in each nostril once daily for adults and children six years of age and older. (b) (4) Omnaris is supplied in an amber glass bottle and provides for nasal delivery with a manual metered pump. Omnaris provides 120 metered sprays after initial priming.

2 METHODS AND MATERIALS

2.1 INTRODUCTION

Since Omnaris was previously approved, DMETS conducted a search of the Agency's Adverse Event Reporting System (AERS) for medication errors associated with the use of Omnaris.

2.2 AERS SELECTION OF CASES

DMETS searched (AERS) using the trade name "Omnaris," and the verbatim term "Omnar%" as well as the MedDRA high level terms "maladministrations", "medication monitoring errors", "medication errors due to accidental exposure", and "medication errors NEC" and the preferred terms "overdose", "accidental overdose", "multiple drug overdose", and "multiple drug overdose accidental".

2.3 MATERIALS REVIEWED

Revised Patient's Instructions for Use and package insert labeling submitted on May 24, 2007.

3 RESULTS

3.1 MEDICATION ERROR CASES

The AERS search did not identify any medication errors associated with the use of Omnaris.

4 DISCUSSION

Our review of the proposed changes to the package insert and Patient's Instructions for Use that include new dosing instructions for 2 to 5 years of age and 6 to 11 years of age identified failure modes where confusion could result in medication errors.

These failure modes are likely to arise in the prescribing, dispensing, and administration phases of the medication use system. For example, errors may occur in the prescribing phase due to the way the dosing is broken down by age groups in the Dosage and Administration section of the package insert and Dosage section in the Patients Instructions for Use. Children (b) (4) 6 to 11 years of age require the same dose as adults, 2 sprays. However, in the labeling, both age groups, patients (b) (4) 6 to 11 years old, are referred to as "children". The age groups for each respective set of dosing only appear in parentheses in aforementioned sections in the labeling, thereby giving the age separation less prominence. Without proper education and prominent labeling, errors in prescribing may go undetected in the dispensing phase. These errors will carry over to the administration phase. Also confusing is that the dosing units are inconsistently presented in the Dosage and Administration section of the package insert and Dosage section in the Patients Instructions for Use. The dosing units mcgs, sprays, and mcg/spray are all used interchangeably. As a result of this inconsistency, errors may arise during prescribing, dispensing, and administration phases because of confusion between the differing dosing units. For instance, a prescriber may refer to the dose in terms of micrograms, however, patients may not be aware of how many micrograms are in each spray and not know what dose to administer or the pharmacist may try to convert the microgram dose to the corresponding number of sprays. These inconsistencies in the labeling often carry over to prescribing practices.

Additionally, upon review of the Patient's Instructions for Use and package insert labeling we noted, as written; it may be difficult for patients to follow the instructions for use. The steps are written in paragraph format which makes them difficult to follow. Illustrations are often helpful to explain instructions for use. In this case, it may be beneficial for all the steps in the use process, including preparation and cleaning to be presented in a format that is more easily understood. Figures illustrating correct use should be used wherever possible along with its corresponding written instructions. Additionally, these instructions should be written in consumer friendly language. Illustrations and consumer friendly language should help to reduce the potential for misunderstanding the directions for use.

5 CONCLUSIONS AND RECOMMENDATIONS

Following the review of the labeling using Failure Mode and Effects Analysis (FMEA) and applying principals of human factors we have identified areas of needed

improvement to ensure the safe use of the product. To minimize the potential for medication errors we recommend the following:

5.1 PATIENT'S INSTRUCTIONS FOR USE LABELING

5.1.1 Ensure that the Patient's Instructions for Use have been submitted to the Division of Surveillance, Research, and Communication Support for review and comment on the comprehensibility.

5.1.2 Include a figure illustrating step #2 in the "Preparing for Use" subsection.

5.1.3 Include a figure illustrating step #1 in the "Applicator Cleaning Instructions" subsection.

5.1.4 "Using the Spray" Section – Revise step #6 to read "Repeat steps 3-5 for each additional spray."

5.2 PACKAGE INSERT LABELING

5.2.1 Revise all dosing instructions so that doses are referred to in number of sprays per nostril rather than mcgs or micrograms per spray.

5.2.2 Revise the Dosage and Administration section of the package insert and the Dosage section of the Patients Instructions for Use so that the age groups are displayed more prominently. For example:

For Adults and Children 6 Years of Age and Older: The recommended dose is 2 sprays in each nostril once daily.

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. Please copy DMETS on any communication to the sponsor with regard to this review. If you have further questions or need clarifications, please contact Cheryl Campbell, project manager, at 301-796-0723.

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

/s/

Kristina Arnwine
11/19/2007 04:10:54 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
11/19/2007 04:45:44 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
11/19/2007 04:47:13 PM
DRUG SAFETY OFFICE REVIEWER

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

MEMORANDUM

Pre-Decisional Agency Information

Date: June 29, 2007

To: Colette Jackson – Regulatory Project Manager
Division of Anesthesia, Analgesia, and Rheumatology Products

From: Michelle Safarik, PA-C – Regulatory Review Officer
Division of Drug Marketing, Advertising, and Communications (DDMAC)

Subject: DDMAC labeling comments for Omnaris (ciclesonide) Nasal Spray, 50 mcg
NDA 22-124

DDMAC has reviewed the revised proposed product labeling (PI) and revised proposed Patient's Instructions for Use for Omnaris (ciclesonide) Nasal Spray, 50 mcg (Omnaris) submitted for consult on June 26, 2007.

Reference is made to an Approval Letter dated October 20, 2006, for Omnaris (NDA 22-004). (b) (4)

DDMAC acknowledges that the following sections of the proposed PI for NDA 22-124 have been updated: Pharmacodynamics, Clinical Trials, Indications and Usage, Pediatric Use, Adverse Events, and Dosage and Administration. We also acknowledge that the proposed PI for NDA 22-124 as well as new onset of action data will be submitted as a prior approval labeling supplement to NDA 22-004 "in the near future."

DDMAC has reviewed the entire label and thus may be commenting on sections of the label that are already approved. We offer the following comments.

PI

Clinical Trials

Pediatric Patients Aged 6 to 11 Years

1. While there were two trials (2-week SAR, 6-week PAR) that evaluated efficacy in pediatric patients aged 6 to 11 years, only the 2-week SAR trial demonstrated a statistically significant difference from placebo. Is this one trial considered substantial evidence to support Omnaris use in pediatric patients aged 6 to 11 years for SAR? If not, we recommend deletion.

(b) (4)

Indications and Usage

1. "OMNARIS Nasal Spray is indicated for the treatment of nasal symptoms associated with seasonal and perennial allergic rhinitis in adults and adolescents (b) (4) years of age and older."

   Based on the patient populations studied and the results from the clinical trials, we recommend revising the indication to the following:

(b) (4)

2 Page(s) of Draft Labeling have been Withheld in Full following this page as B4 (CCI/TS)

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

/s/

Michelle Safarik
6/29/2007 04:50:06 PM
DDMAC REVIEWER