CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-372/S008/S010

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:	February 29, 2008
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Subject:	Aloxi Labeling Supplement
Drug Name(s):	Aloxi (Palonosetron HCL Injection)
Submission Number:	SE1-008 (b) (4) SE1-010
Application Type/Number:	NDA 21-372
Applicant/sponsor:	Helsinn Healthcare
OSE RCM #:	2008-232

CONTENTS

EXECUTIVE SUMMARY

DMETS' analysis of the container, carton and insert labeling noted improvements that should be made to the container label and carton labeling to decrease the potential for selection errors, mimimize confusion with dosing, and increase readability of information presented on the labeling. Such improvements include changing the color of the carton and the proprietary name for the 0.075 mg/1.5 mL strength to differentiate it from the color on the current 0.25 mg/5 mL strength. In addition, the proprietary name should be the same solid color on both the carton and container. For full recommendations, we refer you to section 5 of this review.

1 BACKGROUND

1.1 INTRODUCTION

This review was written in response to a request from the Division of Gastroenterology Products (DGP) to evaluate the container label and labeling supplement for Aloxi (palonosetron HCL) intravenous injection, 0.075 mg/1.5 mL (0.05 mg/mL) for the prevention of postoperative (b) (4) (b) (4) nausea and vomiting (PONV/PDNV) for up to (b) (4)

1.2 REGULATORY HISTORY

Aloxi was approved on July 25, 2003 and is currently indicated for: (1) the prevention of acute nausea and vomiting associated with initial and repeat courses of moderately and highly emetogenic cancer chemotherapy, and (2) the prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy. Aloxi is currently supplied as a 0.25 mg/5 mL (0.05 mg/mL) single-use vial for intravenous injection.

1.3 PRODUCT INFORMATION

Aloxi (palanosetron HCL) is a 5-HT3 receptor antagonist with a strong binding affinity for this receptor and weak affinity for other receptors. Aloxi is currently indicated for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer therapy and for acute nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer therapy. The recommended dose for adults is a single 0.25 mg intravenous dose administered over thirty seconds approximately thirty minutes before the start of chemotherapy. The safety and effectiveness in patients below the age of 18 years has not been established.

The sponsor's proposed indication for Aloxi is the prevention of postoperative (b) (4) nausea and vomiting (PONV (b) (4) up to (b) (4) The dosage for adults is 0.075 mg administered as a single dose intravenously over ten seconds immediately before induction of anesthesia. Aloxi is not indicated for patients under the age of 18.

Aloxi will be available as 0.25 mg/5 mL (0.05 mg/mL) and 0.075 mg/1.5 mL (0.05 mg/mL) single-use intravenous vials. Aloxi is stored at room temperature (20°C-25°C) and should be protected from light.

2 METHODS AND MATERIALS

This section describes the methods and materials used by the DMETS medication error staff to conduct a label, labeling, and/or packaging risk assessment (see section 3 Results). The primary focus of the assessments is to identify and remedy potential sources of medication errors prior to drug approval. DMETS defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The carton and container labels communicate critical information including the proprietary and established name, strength, form, container quantity, expiration date, and so on. The insert labeling is intended to communicate to practitioners all the information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program (MERP) may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.[2]

DMETS staff analyzes reported misuse of drugs and are able to use their experience to identify potential errors with all packaged, labeled and/or prescribed medications. DMETS uses failure mode and effects analysis (FMEA) and human factor principles to identify potential sources of error with the proposed product labels and insert labeling. DMETS then provides recommendations that aim at reducing the risk of medication errors.

2.1 ADVERSE EVENT REPORTING SYSTEM

Because Aloxi has been marketed since 2003, DMETS conducted a search of the Adverse Event Reporting System (AERS) database to determine if any medication errors are associated with the use of Aloxi. The MedDRA Higher Level Terms (HLT) "Maladministration", "Medication Errors NEC", "Medication Errors Due to Accidental Exposures", "Medication Monitoring Errors", and the Preferred Terms (PT) "Overdose", "Accidental Overdose", "Multiple Drug Overdose", "Multiple Drug Overdose Accidental", and verbatim substance names "Alox%" and "Palonos", tradename "Aloxi", and active ingredient "Palonosetron" were used as search criteria.

The cases were manually reviewed to determine if a medication error occurred. Those cases that did not describe a medication error were excluded from further analysis. The cases that did describe a medication error were categorized by type of error. DMETS reviewed the cases within each category to identify factors that contributed to the medication errors.

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[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors.html. Last accessed 10/11/2007.

[2] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

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