CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-353

OTHER REVIEW(S)

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

PRE-DECISIONAL AGENCY MEMO

Date: August 31, 2009

To: Margarita Tossa- Regulatory Project Manager
Matthew Sullivan – Regulatory Project Manager
Division of Anesthesia, Analgesia, and Rheumatology Products (DAARP)

From: Mathilda Fienkeng – Regulatory Review Officer
Twyla Thompson – Regulatory Review Officer
Division of Drug Marketing, Advertising, and Communications (DDMAC)

Through: Mike Sauers – Acting Group Leader
Division of Drug Marketing, Advertising, and Communications (DDMAC)

Subject: DDMAC draft labeling comments
NDA 22-353 **COLCRYS™** (Colchicine Tablets, USP) for Oral use

DDMAC has reviewed the proposed product labeling (PI), and Medication Guide for **COLCRYS™** (Colchicine Tablets, USP) for Oral use (Colcrys), submitted for consult on January 6, 2009.

The following comments are provided using the updated proposed PI, and Medication Guide sent via email on August 21, 2009 by Margarita Tossa. If you have any questions about DDMAC's comments, please do not hesitate to contact us.

23 Page(s) Withheld

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

__√__ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

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/s/

MATHILDA K FIENKENG
08/31/2009

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:	August 7, 2009
To:	Bob Rappaport, MD, Director Division of Anesthesia, Analgesia and Rheumatology Products
Through:	Kristina C. Arnwine, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Carol A. Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Loretta Holmes, BSN, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Label Review
Drug Name:	Colcrys (Colchicine, USP) Tablets 0.6 mg
Application Type/Number:	NDA 22-353
Applicant:	Mutual Pharmaceutical Company, Inc.
OSE RCM #:	2009-1224

1 INTRODUCTION

This product was recently approved on July 29, 2009 and July 30, 2009, respectively, for the treatment of familial Mediterranean fever (NDA 22-352) and the treatment of gout flares (NDA 22-351). Although the container labels were approved as part of these NDAs, the Division of Anesthesia, Analgesia and Rheumatology Products (DAARP) requested a review of the container labels for the prevention of gout flares indication of use (NDA 22-353).

2 METHODS AND MATERIALS

The Division of Medication Error Prevention and Analysis (DMEPA) used principles of Human Factors and Failure Mode and Effects Analysis (FMEA) in our evaluation of the following labels submitted as part of the July 23, 2009 submission under NDA 22-351 and NDA 22-352 (see Appendix A). We note the Applicant did not cross reference this NDA 22-353, nor did they submit revised labels to this NDA.

- Container Labels: 30-, 60-, 100-, 250-, 500-, and 1000-count bottles

3 RECOMMENDATIONS

Our evaluation noted an area where information on the container labels can be improved to minimize the potential for medication errors. Section 3.1 *Comments to the Applicant* contains our recommendation for the container labels. We request the recommendation in Section 3.1 be communicated to the Applicant prior to approval.

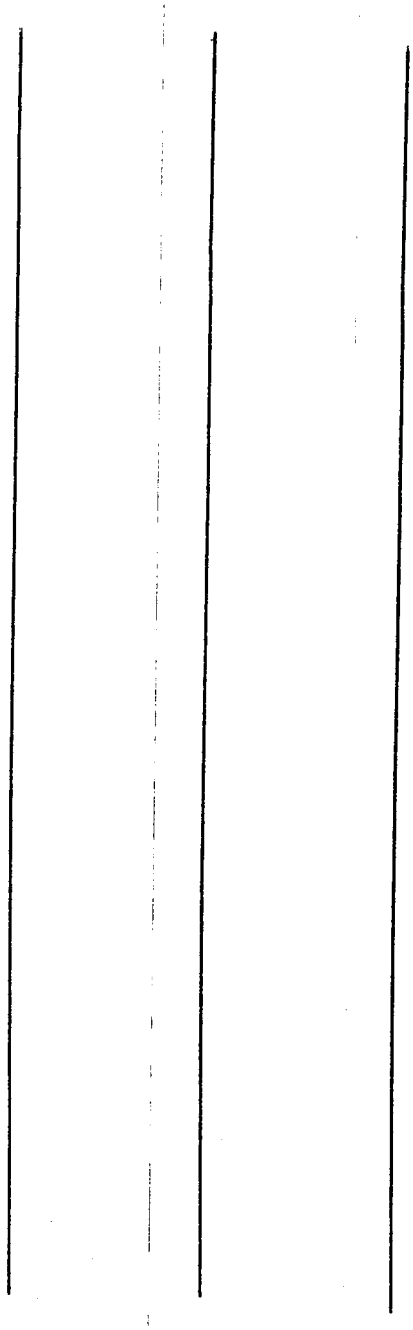
We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention and Analysis on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact OSE Regulatory Project Manager, Chris Wheeler, at 301-796-0151.

3.1 COMMENTS TO THE APPLICANT

As previously noted in the Agency's February 20, 2009 e-mail containing our label and labeling comments, the established name is not at least ½ the size of the proprietary name. The size of the established name should be increased to at least ½ the size of the proprietary name (taking into account all pertinent factors, including typography, layout, contrast, and other printing features) in order to comply with 21 CFR 201.10(g)(2). We recommend decreasing the size of the manufacturer's logo and the "Rx" symbol, at the bottom of the container label, to allow more space to increase the prominence of the established name.

APPENDICES

Appendix A Container Labels



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/s/

LORETTA HOLMES
08/07/2009

KRISTINA C ARNWINE
08/07/2009

DENISE P TOYER
08/07/2009

Risk Evaluation and Mitigation Strategy (REMS) Memorandum

U.S. FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
Office of Drug Evaluation II
Division of Anesthesia, Analgesia and Rheumatology Products

NDA:	NDA 022353
PRODUCT:	Colcrys (colchicine, USP)
SPONSOR:	Mutual Pharmaceuticals
FROM:	Rigoberto Roca, M.D. Deputy Director, DAARP
DATE:	October 16, 2009

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the Federal Food, Drug, and Cosmetic Act (FDCA) to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)(1)). Section 505-1(a)(1) provides the following factors:

A. The estimated size of the population likely to use the drug involved;
B. The seriousness of the disease or condition that is to be treated with the drug;
C. The expected benefit of the drug with respect to such disease or condition;
D. The expected or actual duration of treatment with the drug;
E. The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug;
F. Whether the drug is a new molecular entity.

The parent NDA (NDA 022352), approved on July 29, 2009, provided for the use of Colcrys (colchicine) for the treatment of familiar Mediterranean fever (FMF). After

consultations between the Office of New Drugs and the Office of Surveillance and Epidemiology, we have determined that a REMS is necessary for Colcrys (colchicine, USP) to ensure that the benefits of the drug outweigh the risks of increased susceptibility to colchicine toxicity in patients with renal or hepatic impairment and fatal drug-drug interactions involving strong P-glycoprotein (P-gp) inhibitors. A Medication Guide only REMS was required for NDA 022352. In reaching this determination we considered the following:

A. Familial Mediterranean fever (FMF) is an orphan indication, and is estimated to affect approximately 5000 patients in the US.

B. FMF, if untreated, is associated with end-organ damage and premature mortality as a consequence of uncontrolled inflammation (i.e., secondary amyloidosis).

C. Colcrys (colchicine, USP) is the only known efficacious treatment for FMF.

D. Patients with FMF must remain on Colcrys (colchicine, USP) treatment chronically (i.e., life-long) in order to prevent recurrent inflammatory attacks.

E. Although the toxicity of Colcrys (colchicine, USP) is well known and described in the medical literature including risks of blood dyscrasias, neuromuscular toxicity, and severe gastrointestinal toxicity, the number of patients reported with fatal non-overdose colchicine toxicity related to clarithromycin (60/117 or 51% of non-overdose fatalities reported to AERS through June 30, 2007) suggests that the severity of the potential interaction between colchicine and clarithromycin may not be widely understood. Patient awareness of potential serious drug-drug interactions with colchicine is especially important, since clarithromycin may be prescribed by different healthcare providers seeing the patient for an acute illness and, likewise, a healthcare provider seeing the patient for chronic conditions may not be aware of a new prescription for clarithromycin given for an acute illness.

F. Colcrys (colchicine, USP) is not a new molecular entity.

On July 30, 2009, NDA 022351, for the use of Colcrys (colchicine) for the treatment of gout flares, was approved. The REMS is identical to the REMS approved on July 29, 2009 under the parent NDA 022352.

NDA 022353 provides for the use of Colcrys (colchicine) for the prophylaxis of gout flares. The REMS is identical to the REMS approved on July 29, 2009 under the parent NDA 022352.

In accordance with section 505-1 of the FDCA and under 21 CFR Part 208, FDA has determined that a Medication Guide is required for Colcrys (colchicine, USP). FDA has determined that Colcrys (colchicine, USP) poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Colcrys (colchicine). FDA has determined that Colcrys (colchicine) is a product for which patient labeling could help prevent serious adverse effects and that has serious risks (relative to benefits) of which

patients should be made aware because information concerning the risks could affect patients' decision to use, or continue to use, Colcrys (colchicine, USP).

The elements of the REMS will be a Medication Guide and a timetable for submission of assessments of the REMS.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22353	ORIG-1	MUTUAL PHARMACEUTICAL CO INC	COLCHICINE TABLETS USP 0.6MG

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/s/

SARA E STRADLEY
10/16/2009

RIGOBERTO A ROCA
10/16/2009