

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
022424Orig1s000

OTHER REVIEW(S)

**FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion**

*****Pre-decisional Agency Information*****

Memorandum

Date: April 28, 2015

To: Laura Musse, Regulatory Project Manager
Division of Pulmonary, Allergy, and Rheumatology Products
(DPARP)

From: Roberta Szydlo, Senior Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Kathleen Klemm, Team Leader, OPDP

Subject: NDA 022424
OPDP labeling comments for Flowtuss (hydrocodone bitartrate and
guaifenesin) Oral Solution CII

In response to DPARP's consult request dated December 22, 2014, (DARRTS check-in date April 24, 2015), OPDP has reviewed the draft labeling (Package Insert [PI] and Carton/Container Labeling) for Flowtuss (hydrocodone bitartrate and guaifenesin) Oral Solution CII (Flowtuss).

PI:

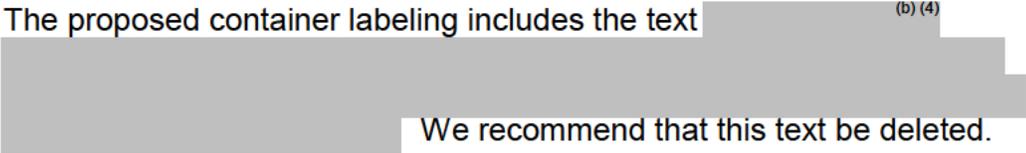
OPDP's comments on the PI are provided directly below and are based on the draft labeling titled "NDA 22424 PI SCPI.doc" (attached) that was provided via email from DPARP on April 16, 2015.

Carton/Container Labeling:

OPDP has reviewed the proposed container labeling submitted by the sponsor on February 19, 2015 (attached) and available at:

- <\\cdsesub1\evsprod\nda022424\0022\m1\us\114-labeling\1142-final-label\11421-final-cart-cont-label\114212-final-label-16oz-0022-amend.pdf>
- <\\cdsesub1\evsprod\nda022424\0022\m1\us\114-labeling\1142-final-label\11421-final-cart-cont-label\114211-final-label-4oz-0022-amend.pdf>

We offer the following comments:

- The proposed container labeling includes the text (b) (4)
 We recommend that this text be deleted.
- We recommend that the established name be presented in a manner consistent with 21 CFR 201.10(g)(2) which requires that the established name be at least half the size of the letters comprising the proprietary name and have a prominence consistent with the proprietary name in terms of type, size, color, and font.

Thank you for your consult. If you have any questions, please contact Roberta Szydlo at (301) 796-5389 or roberta.szydlo@fda.hhs.gov.

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/s/

ROBERTA T SZYDLO
04/28/2015

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	March 5, 2015
Requesting Office or Division:	Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)
Application Type and Number:	NDA 022424
Product Name and Strength:	Flowtuss (Hydrocodone Bitartrate and Guaifenesin) Oral Solution, 2.5 mg/200 mg per 5 mL
Product Type:	Multi-ingredient Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Mikart Inc.
Submission Date:	February 19, 2015
OSE RCM #:	2014-2613
DMEPA Primary Reviewer:	Lissa C. Owens, PharmD
DMEPA Team Leader:	Kendra Worthy, PharmD

1 REASON FOR REVIEW

This review evaluates the proposed container label and prescribing information, for Flowtuss for risk of medication error in response to a request from the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP). DPARP requested this as part of their evaluation for NDA 022424.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Label and Labeling Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
FDA Adverse Event Reporting System (FAERS)	N/A
Previous DMEPA Reviews	N/A
Human Factors Study	N/A
ISMP Newsletters	N/A
Other	N/A
Labels and Labeling	G

N/A=not applicable for this review

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Hydrocodone Bitartrate and Guaifenesin are currently marketed individually and in combination in different products, strengths, and formulations. This submission is a 505(b)(2) application.

We performed a risk assessment of the proposed container label and insert labeling, to identify deficiencies that may lead to medication errors.

DMEPA finds the proposed insert labeling is acceptable. However, the container label can be improved to increase the readability of the label.

4 CONCLUSION & RECOMMENDATIONS

DMEPA concludes that the proposed container labels can be improved to increase the readability of important information on the label.

Based on this review, DMEPA recommends the following be implemented prior to approval of this NDA:

4.1 RECOMMENDATIONS FOR THE APPLICANT

A. All Container Labels

1. Revise the presentation of the proprietary name from all caps (i.e. FLOWTUSS) to title case (i.e. Flowtuss) to improve readability of the name. Words set in title case are easier to read than the rectangular shape that is formed by words set in all capital letters.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Flowtuss that Mikart Inc. submitted on February 19, 2015.

Table 2. Relevant Product Information for Flowtuss	
Initial Approval Date	N/A
Active Ingredient	Hydrocodone Bitartrate and Guaifenesin
Indication	Symptomatic relief of cough and to loosen mucus associated with the common cold
Route of Administration	Oral
Dosage Form	Solution
Strength	2.5 mg/200 mg per 5mL
Dose and Frequency	10 mL every 4 to 6 hours, not to exceed 6 doses (60 mL) in 24 hours
How Supplied	Violet-colored, black raspberry flavored liquid available in bottles of 4 fl. Oz. (118 mL) and 16 fl. oz. (473 mL)
Storage	Store at 20°C - 25°C (68°F - 77°F)

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,¹ along with postmarket medication error data, we reviewed the following Epinephrine Injection labels and labeling submitted by Mikart Inc. on February 19, 2015.

- Container label
- Full Prescribing Information

G.2 Label and Labeling Images

(b) (4)



¹ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.



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/s/

LISSA C OWENS
03/05/2015

KENDRA C WORTHY
03/05/2015

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: February 04, 2015

TO: Division of Pulmonary, Allergy, and Rheumatology Products

FROM: Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Recommendation to accept data without on-site inspection**

RE: NDA 022424 and NDA 022279

The Division of New Drug Bioequivalence Evaluation (DNDBE) within the Office of Study Integrity and Surveillance (OSIS) recommends accepting data without an on-site inspection. The rationale for this decision is noted below.

OSIS inspected the site listed below within the last four years. The inspectional outcomes from the inspections were classified as No Action Indicated (NAI).

Requested Site Inspection

Facility Type	Facility Name	Facility Address
Analytical	(b) (4)	
Clinical	Novum Pharmaceutical Research Services	3760 Pecos McLeod, Las Vegas, NV, 89121

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/s/

SHILA S NKAH
02/04/2015