

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

ANDA 40-458

ADMINISTRATIVE DOCUMENTS



DEPARTMENT OF HEALTH & HUMAN SERVICES
Food and Drug Administration

Memorandum

DATE: May 21, 2002

FROM: Supervisory Chemist, Drug Chemistry Branch
Northeast Regional Laboratory, HFR-NE560

SUBJECT: ANDA 40-458: Carbinoxamine Maleate
Mikart, Inc.; Atlanta, GA 30318
Sample No. 168545

TO: Nashed E. Nashed, Ph.D., Review Chemist
Office of Generic Drugs, CDER, HFD-627


Through: Diane O'Brien, MV Coordinator
Division of Field Science, HFC-140

The analysis of Carbinoxamine Maleate _____, 4mg/5mL, was performed by the Northeast Regional Laboratory using the firm's method and the samples provided. The following is a summary of the analysis.

Liquid	Results	Specifications
Assay: carbinoxamine Maleate	ave % of declared = _____	_____
Assay: methyparaben	Ave. found = _____	_____
Assay: propylparaben	Ave. found = _____	_____
Related Substances: unknown Total	_____ _____	NMT _____ individual NMT _____ total

A second placebo sample was requested and received, because the original placebo contained the active ingredient. The peak calculated as an unknown impurity was not present in the blank or the placebo. The placebo received had no peaks, although the method description lists the rrt for several peaks in the placebo. The placebo received appears to be a blank. This peak also appears to be the same peak seen in the firm's chromatograph, which is not calculated as an impurity. From the placebo received, we could not exclude this peak as an impurity.

No major problems were encountered with the firm's method for this product. The method appears to be suitable for regulatory analysis of this product.


Ella S. Walker
Supervisory Chemist
Northeast Regional Lab
(718) 340-7008

Sample received: 04/22/02
Sample analysis completed: 05/10/02
Lab Classification: 1

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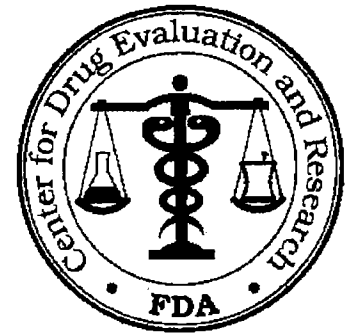
CORRESPONDENCE

MINOR AMENDMENT

ANDA 40-458

MAR 14 2002

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)



TO: APPLICANT: Mikart, Inc.

TEL: 404-351-4510

ATTN: Cerie B. McDonald

FAX: 404-350-0432

FROM: Sarah Ho

PROJECT MANAGER: 301-827-5754

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated November 15, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Carbinoxamine Maleate — 4 mg/5 mL.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (3 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

CMC and Bioequivalency comments provided. Please include in your response.

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October 17, 2002

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT

N/A M

Re: ANDA 40-458 MINOR AMENDMENT
Carbinoxamine Maleate — 4 mg/5 mL

Dear Sir/Madam:

Reference is made to the Agency's March 14, 2002 Not Approvable Letter for the application listed above. Reference is also made to Mikart Inc.'s abbreviated new drug application dated November 15, 2001.

Mikart, Inc. herein submits a complete and full response to all items listed in the Not Approvable Letter. To assist in the review of the submission, each Agency comment is reprinted in bold type followed by the sponsor's point-by-point response. A copy of the Agency's Not Approvable Letter dated March 14, 2002 is also included.

This submission also includes an unsolicited amendment related to Mikart's intended use of another outside testing facility for future production. This amendment is included in Attachment 6.

Thank you for your attention to the review of this material. If you have any questions or comments regarding this submission please contact Valerie Cutrale, Regulatory Submissions at (404) 351-4510.

Sincerely,

Cerie B. McDonald
President

CBM:vc

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OCT 21 2002

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Chattahoochee Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

Handwritten initials/signature



November 21, 2002

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/AM

Re: AMENDMENT TO UNAPPROVED ANDA 40-458
Carbinoxamine Maleate —, 4 mg/5 mL

Dear Sir/Madam:

Reference is made to Mikart Inc.'s abbreviated new drug application dated November 15, 2001. Reference is also made to Mikart's Minor Amendment dated October 17, 2002 and Mikart's Unsolicited Amendment dated October 17, 2002.

Ms. Sarah Ho, Project Manager OGD, telephoned Mikart on November 20, 2002 to request that Mikart submit formal statements to withdraw the contract _____ from the subject ANDA and to add _____ to the subject ANDA.

Mikart, Inc., herewith, submits the documents requested. A cGMP compliance statement for _____ and other relevant documents and information are included in Mikart's October 17, 2002 Unsolicited Amendment (submitted as an attachment to Mikart's Minor Amendment also dated October 17, 2002).

Thank you for your attention to the review of this material. If you have any questions or comments regarding this submission please contact Valerie Cutrale, Regulatory Submissions at (404) 351-4510.

Sincerely,

*Robert J. Groenewald for
Cerie B. McDonald*

Cerie B. McDonald
President

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NOV 22 2002

OGD / CDER

CBM:vc



ORIG AMENDMENT

N/AM

December 9, 2002

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: TELEPHONE AMENDMENT TO UNAPPROVED ANDA 40-458
Carbinoxamine Maleate 4 mg/5 mL

Dear Sir/Madam:

Reference is made to Mikart Inc.'s abbreviated new drug application dated November 15, 2001. Reference is also made to Mikart's Minor and Unsolicited Amendments both dated October 17, 2002.

Ms. Sarah Ho, Project Manager OGD, and an Agency designated Chemistry Reviewer (un-named) jointly telephoned Mikart on December 6, 2002 to request clarification and supporting documentation regarding two chemistry review items:

1. The drug substance specification should be revised to include particle size, and a revised COA for the raw material should be issued.
2. The stability data summary reports should be updated to reflect the current, impurity <related substances> specification.

Mikart, Inc., herewith, responds to the Agency's inquiry; the items are reprinted in bold followed by the sponsor's point by point response. Thank you for your attention to the review of this material. If you have any questions or comments regarding this submission please contact Valerie Cutrale, Regulatory Submissions at (404) 351-4510.

Sincerely,

Cerie B. McDonald
President

CBM:vc

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ORIG AMENDMENT

NIAF

March 13, 2003

Office Of Generic Drugs, CDER, FDA
Document Control Room,
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: MINOR AMENDMENT - Labeling Deficiency Response
ANDA 40-458
Carbinoxamine Maleate Oral Solution, 4 mg/5mL

Dear Sir/Madam:

Reference is made to the Office of Generic Drugs, Division of Labeling (Ms. Debra Catterson) January 17, 2003 telephone communication regarding labeling deficiencies for the subject ANDA. Reference is also made to Mikart, Inc.'s abbreviated new drug application dated November 15, 2001.

Mikart, Inc. herein submits a full and complete response to the items communicated by Ms. Catterson during the January 17, 2003 teleconference. Ms. Catterson advised Mikart that a written labeling deficiency notice would not follow the telephone communication. Ms. Catterson's comments are listed below:

1. Change the product name from _____ to Oral Solution throughout the insert and container labeling.
2. Revise Each 5mL contains carbinoxamine maleate, 4 mg to
Each 5 mL (teaspoonful) contains carbinoxamine maleate, USP 4 mg
3. Move the inactive ingredients list to follow the chemical formula of the active
4. revise citric acid to citric acid anhydrous
5. revise sodium citrate to sodium citrate hydrous
6. otherwise, use the RLD tablet model, McNeil Lab version 7/17/85, for all other sections

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MAR 14 2003

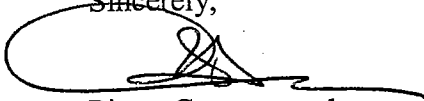
OGD / CDER

Mikart, Inc. • Pharmaceutical Manufacturers
1750 Northchase Avenue • Atlanta, Georgia 30318
404-351-4510 • Fax 404-350-0432

Mikart's proposed final print insert and container labeling are submitted herein. The container labeling side by side reflects comparison of Mikart's previously submitted draft container labeling with the proposed final print labeling for three packaging sizes. The package insert side by side reflects comparison of the most current insert labeling for the reference listed drug, Clistin® (carbinoxamine maleate) Tablets, rev. 7/17/85 and Mikart's proposed final print labeling for Carbinoxamine Maleate Oral Solution, 4 mg/5mL. Twelve copies of each label are submitted.

Thank you for your attention to the review of this material. If you have any questions or comments regarding this submission, please contact Valerie Cutrale, Regulatory Submissions (404) 351-4510.

Sincerely,



Pieter Groenewoud
Vice President of R&D

PG: vc