CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 40-458

LABELING REVIEW(S)

APPROVAL SUMMARY

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-458

Date of Submission: March 13, 2003 (Amendment-FPL) and November 15, 2001 (original)

Applicant's Name: Mikart, Inc.

Established Name: Carbinoxamine Maleate Oral Solution, 4 mg/5 mL

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes.

CONTAINER Labels: [Bottles of 1 oz. (Professional Sample), 4 oz., and 16 oz.]:
Satisfactory as of the March 13, 2003 submission. [Vol. 2.1, "Attachment 1", Rev. 01/03]

PROFESSIONAL PACKAGE INSERT:
Satisfactory as of the March 13, 2003 submission. [Vol. 2.1, "Attachment 2", Rev. 01/03]

Revisions needed post-approval: None.

Patent Data – NDA 08-955

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 08-955

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

BASIS OF APPROVAL:

Was this approval based upon a petition? Yes.

What is the RLD on the 356(h) form: Clistin® Elixir

NDA Number: 08-955

NDA Drug Name: Carbinoxamine Maleate Elixir

NDA Firm: McNeil Pharmaceutical, Inc.

Date of Approval of NDA Insert and supplement: This NDA was withdrawn on May 6, 1985. The last labeling supplement submitted by the innovator (SLR-008) was approved on April 1, 1980. I was

unable to locate the labeling for this supplement, S-008, because of its age and the fact that the NDA was withdrawn. However, I was able to locate a copy of Clistin® Tablets labeling, from a July 20, 1988 annual report (Vol. 9.1 in the HFD-570 Document Room, Parklawn Bldg.), with a revision date of July 17, 1985. I asked the firm to revise their labeling to be in accord with this July 17, 1985 labeling for Clistin® Tablets.

Has this been verified by the MIS system for the NDA? Yes.

Was this approval based upon an OGD labeling guidance? No.

Basis of Approval for the Container Labels: Clistin® Tablets container labeling from a July 20, 1988 annual report (Vol. 9.1 in the HFD-570 Document Room, Parklawn Bldg.), with a revision date of Jul. 17, 1985.

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Applicant's Established Name	Yes	No	N/A
Different name than on acceptance to file letter?	X		
Is this product a USP item? If so, USP supplement in which verification was assured.	X		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?		x	
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			X
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			X
PACKAGING -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA for this drug product? If yes, describe in FTR.	X		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. [see FTR]		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		x	

Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		x	
LABELING			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?		x	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		x	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		x	
Scoring: Describe scoring configuration of RLD and applicant (p. #) in the FTR			
Is the scoring configuration different than the RLD?		x	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?		x	
Inactive Ingredients: (FTR: List p. # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		x	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?[see FTR]		x	

Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?	X		
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		x	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state. **NONE.**			

FOR THE RECORD:

1. MODEL LABELING

This review was based on the labeling for Clistin® Tablets by McNeil Pharmaceutical (NDA 08-915). The Clistin® Elixir NDA was withdrawn on May 6, 1985. The last labeling supplement submitted by the innovator (SLR-008) for Clistin® Elixir was approved on April 1, 1980. I was unable to locate the labeling for this supplement, S-008, because of its age and the fact that the NDA was withdrawn. However, I was able to locate a copy of Clistin® Tablets labeling, from a July 20, 1988 annual report (Vol. 9.1 in the HFD-570 Document Room, Parklawn Bldg.), with a revision date of July 17, 1985. I asked the firm to revise their labeling to be in accord with this July 17, 1985 labeling for Clistin® Tablets.

2. PATENTS/EXCLUSIVITIES

Patent Data – NDA 08-955

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 08-955

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

The firm's statements are correct. [Vol. A1.1 pg. 9-13.]

3. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM

Mikart, Inc.
2090 Marietta Blvd.
Atlanta,.GA 30318 [Vol. A1.2 pg. 234]

4. CONTAINER/CLOSURE

1 oz: 1 oz. [redacted] Round, smooth-sided, opaque-white HDPE bottle, with [redacted] white [redacted] child-resistant cap.
4 oz: 4 oz [redacted] Round, smooth-sided, opaque-white HDPE bottle, with [redacted] white [redacted] child-resistant cap.
16 oz: 16 oz. [redacted] oblong, recessed-panel, opaque-white HDPE bottle, with [redacted] white [redacted] child-resistant cap.
[Vol. A1.2 pg. 448-449]

5. INACTIVE INGREDIENTS

The description of the inactive ingredients in the insert labeling appears accurate according to the composition statement. [Vol. A1.1 pg. 85.]

6. PACKAGING CONFIGURATIONS

RLD: Unknown. (Product was withdrawn in 1985 and does not appear in any of our old PDR's)
ANDA: Bottles of 1 oz. (Professional Sample), 4 oz., and 16 oz.

7. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

USP: Preserve in tight, light-resistant containers.
RLD: Store at room temperature (Tablets).
ANDA: Store at controlled room temperature 15°- 30°C (59°- 86°F) (See USP).
The firm has submitted the appropriate 3-month controlled room temperature stability data (25°C to 30°C, Ambient humidity) to support the use of the above storage statement. [See Vol.1.3, pages 720-722.]

8. DISPENSING STATEMENTS COMPARISON

USP: None
RLD: Dispense in tight, light-resistant container as defined in the official compendium. This is a bulk container. Not intended for household use. [Tablets]
ANDA:PHARMACIST: Dispense in a tight, light-resistant container with a child-resistant closure.

9. DESCRIPTION OF FINISHED PRODUCT

The description of the finished product has been accurately described in the HOW SUPPLIED section of the insert labeling according to the firm's Finished Product Specifications:

"Clear, colorless liquid with a bubble gum aroma."

[Vol. A1.3 pg. 722]

10. BIOAVAILABILITY/BIOEQUIVALENCE:

The Division of Bioequivalence concluded on February 14, 2002, that the firm's bioequivalence study data were acceptable.

Date of Review: 3/28/03 Dates of Submission: 3/13/03 and 11/15/01

Primary Reviewer: Debra Catterson Date:

Debra M. Catterson 3/31/03

Team Leader: John Grace Date:

3/31/03

cc:

ANDA: 40-458
DUP/DIVISION FILE
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Review