CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-602

ADMINISTRATIVE DOCUMENTS

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

ANDA Number: 75-602 Date of Submission: March 21, 2000

Applicant's Name: Mikart, Inc.

Established Name: Aminocaproic Acid Tablets USP, 500 mg

Labeling Deficiencies:

INSERT

a. PRECAUTIONS

i. General

Replace the last paragraph with the following.

> Epsilon-aminocaproic acid should not be administered with Factor IX Complex concentrates or Anti-Inhibitor Coagulant concentrates, as the risk of thrombosis may be increased.

ii. Pregnancy

Delete "Tablets USP" from the second sentence.

b. ADVERSE REACTIONS (Special Senses)

Capitalize the "t" in "tinnitus" for consistency.

Please revise your insert labeling as instructed above and submit 12 final printed copies of container label and package insert labeling.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes –

http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING
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Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
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APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

- Do you have 12 Final Printed Labels and Labeling?
- Container Labels:
- Professional Package Insert Labeling:
- Revisions needed post-approval:

BASIS OF APPROVAL:

• Was this approval based upon a petition?	No
• What is the RLD on the 356(h) form:	Amicar
• NDA Number:	15-197
• NDA Drug Name:	Amicar
• NDA Firm:	Immunex Corporation
• Date of Approval of NDA Insert and supplement #:	April 3, 2000; S-034
• 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:	Side by Side

FOR THE RECORD:

1. Model Labeling – Amicar, Immunex Corporation, NDA 15-197/S-034, Approved April 3, 2000.

2. Patents/Exclusivities – There are no patents or exclusivities listed in the 19th Edition of the Orange Book.

3. Container/Closure – HDPE bottle with CRC

4. Storage/Dispensing Recommendations
   - USP: Preserve in tight containers.
   - NDA: Store between 15^0-30^0C (59^0-86^0F), Dispense in tight containers.
   - ANDA: Store at controlled room temperature, 15^0-30^0C (59^0-86^0F), Dispense in a tight container with a child-resistant closure.

5. Outside firms are used for product testing only.

6. Component/Composition – Consistent, see page 32.

7. Potential FIRST GENERIC.

8. Description – consistent with application, see page 1715.

9. HOW SUPPLIED section: Firm's statement, "Aminocaproic Acid Tablets USP, which contain aminocaproic acid 500 mg" appears redundant however, it is acceptable. It is the reviewer's opinion that it should read as, "Aminocaproic Acid Tablets USP, 500 mg for oral administration are supplied as..."

Date of Review: August 8, 2000 — Date of Submission: March 21, 2000

Primary Reviewer: Koung Lee — Date: 8/11/00

Team Leader: Charlie Hoppes — Date: 8/11/00

cc.

LABELING

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

ANDA Number: 75-602

Date of Submission: March 17, 1999
Refuse to file date: April 28, 1999
Filing date: May 17, 1999

Applicant's Name: Mikart, Inc.

Established Name: Aminocaproic Acid Tablets USP, 500 mg

Labeling Deficiencies:

1. CONTAINER

Add "(see USP)" after the storage temperature statement.

2. INSERT

a. DESCRIPTION

i. Replace "chemical" with "structural" in the second sentence.

ii. Replace "M.W. 131.18" with "M.W. 131.17"

b. PRECAUTIONS

Add as the last paragraph the following.

> Thrombosis with severe sequelae (acute myocardial infarction, gangrene) has been rarely reported in patients with hemophilia receiving combined treatment with Factor IX concentrate and aminocaproic acid. Aminocaproic acid should not be administered concomitantly with prothrombin complex concentrates or with activated prothrombin concentrates unless the increased risk of thrombosis is outweighed by the anticipated clinical benefit.

c. ADVERSE REACTIONS (Urogenital)

i. Delete "ejaculatory disorder" from the first sentence.

ii. Add "been" between "These have" and "reported to date".

iii. Add "of completion" between "24 to 48 hours" and "of therapy."

d. OVERDOSAGE

Delete the comma between "tumor and seizures" and "experienced seizures after".

e. HOW SUPPLIED

See CONTAINER comment.

Please revise your label and labeling as instructed above and submit 12 final printed copies of container label and package insert labeling.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes –

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To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

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

- Do you have 12 Final Printed Labels and Labeling?
- Container Labels:
- Professional Package Insert Labeling:
- Revisions needed post-approval:

BASIS OF APPROVAL:

• Was this approval based upon a petition?	No
• What is the RLD on the 356(h) form:	Amicar
• NDA Number:	15-197
• NDA Drug Name:	Amicar
• NDA Firm:	Immunex Corporation
• Date of Approval of NDA Insert and supplement #:	March 3, 1998, S-030
• 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:	Side by Side

REVIEW OF PROFESSIONAL LABELING CHECK LIST

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. USP 23	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			
Is this a new packaging configuration, never been approved by an ANDA or NDA? 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.		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	
Labeling(continued)	Yes	No	N.A.
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 (page #) 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 page # 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?		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.		x	

FOR THE RECORD:

1. Model Labeling – Amicar, Immunex Corporation, NDA 15-197/S-030, Approved April16, 1997.

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3. Container/Closure – HDPE bottle with CRC

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Date of Review: October 29, 1999

Date of Submission: March 17, 1999
Refuse to file date: April 28, 1999
Filing date: May 17, 1999

Primary Reviewer: Koung Lee

Date: 11/1/99

Team Leader: Charlie Hoppes

Date: 11/1/99

cc:

ELING