CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-602

CHEMISTRY REVIEW(S)

38. Chemistry comments to be provided to the applicant

ANDA: **75-602** APPLICANT: **Mikart, Incorporated**

DRUG PRODUCT: Aminocaproic Acid Tablets USP, 500 mg

The following deficiencies represent MINOR deficiencies:

1. DMF is deficient and the holder has been informed.

2. Your specification for in the drug substance is too high compared to your specification for in the finished product and stability specifications.

3. What do you mean by completion of Pharmacy step? Is it the end of weighing of ingredients? Note that start time of manufacturing is the day the active ingredient is mixed with other ingredients.

4. We acknowledge the receipt of your in-process summary production (p 10 of Amendment dated March 21, 2000) and that friability, disintegration, and individual weight variations of 20 units have been removed from the tablet compression master. Please clarify.

5. Please refer to question #5 in the last deficiency letter and clarify if the actual test dates for the 30-day and 60-day time stations are July 24 and July 26, 1996, respectively. Note that scheduled removal date for 30-day and 60-day time stations are June 24 and July 25, 1996, respectively.

6. We acknowledge that the test for related substances was added on the 29th of July 1998. However, no test was conducted at the 36 months time station (April 16, 1999) for lot #B960222. Please explain. In addition, your stability report form should have all the changes such as moisture and specifications for related substances.

Sincerely yours,

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

1. CHEMISTRY REVIEW # 2

2. ANDA # 75-602

3. NAME AND ADDRESS OF APPLICANT
Mikart, Incorporated
Attention: Cerie B. McDonald
1750 Chattahoochee Avenue, N.W.
Atlanta, GA 30318

4. LEGAL BASIS FOR ANDA SUBMISSION
The basis of this submission is the approved listed drug, Amicar® Tablets, 500 mg (NDA #15-197). There are no patent information and exclusivity period for the listed drug (pp 12, 14).

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Aminocaproic Acid

8. SUPPLEMENT PROVIDE FOR:
N/A

9. AMENDMENTS AND OTHER DATES:
March 17, 1999: Original Submission
April 28, 1999: Refuse to File
May 14, 1999: Amendment
May 17, 1999: Acceptable for Filing
October 4, 1999: Bio Review #1
October 29, 1999: Chemistry Review #1
November 1, 1999: Labeling Review #1
March 21, 2000: Amendment

10. PHARMACOLOGICAL CATEGORY
Antifibrinolytic Agent

11. Rx or OTC
Rx

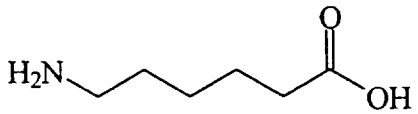
12. RELATED DMFs

13. DOSAGE FORM
Tablet

14. POTENCY
500 mg

15. CHEMICAL NAME AND STRUCTURE

Aminocaproic Acid. $C_6H_{13}NO_2$. 131.18. 6-Aminohexanoic acid



16. RECORDS AND REPORTS
N/A

17. COMMENTS
New comments/deficiencies are in bold.

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable, MINOR

19. REVIEWER
Ijeoma N. Nnamani, Ph.D.

DATE COMPLETED
July 26, 2000

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38. Chemistry comments to be provided to the applicant

ANDA: **75-602** APPLICANT: **Mikart, Incorporated**

DRUG PRODUCT: Aminocaproic Acid Tablets USP, 500 mg

The following deficiencies represent MINOR deficiencies:

1. DMF is deficient and the holder has been informed.

2. Your specification for in the drug substance is too high compared to your specification for in the finished product and stability specifications.

3. What do you mean by completion of Pharmacy step? Is it the end of weighing of ingredients? Note that start time of manufacturing is the day the active ingredient is mixed with other ingredients.

4. We acknowledge the receipt of your in-process summary production (p 10 of Amendment dated March 21, 2000) and that friability, disintegration, and individual weight variations of 20 units have been removed from the tablet compression master. Please clarify.

5. Please refer to question #5 in the last deficiency letter and clarify if the actual test dates for the 30-day and 60-day time stations are July 24 and July 26, 1996, respectively. Note that scheduled removal date for 30-day and 60-day time stations are June 24 and July 25, 1996, respectively.

6. We acknowledge that the test for related substances was added on the 29th of July 1998. However, no test was conducted at the 36 months time station (April 16, 1999) for lot #B960222. Please explain. In addition, your stability report form should have all the changes such as moisture and specifications for related substances.

Sincerely yours,

8/14/00

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

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38. Chemistry comments to be provided to the applicant

ANDA: **75-602** APPLICANT: **Mikart, Incorporated**

DRUG PRODUCT: Aminocaproic Acid Tablets USP, 500 mg

The following deficiencies represent MAJOR deficiencies.

A. Deficiencies:

1. What is the time limit of your manufacturing process?

2. Reported hardness results for both executed batches are in the range of . Please reduce your specified hardness range to reflect results obtained. In addition, correct your blank batch record to reflect the change in the lower limit from .

3. Please include an organoleptic test in your finished product specifications. Also, we require tests and specifications for moisture and hardness in your finished product specifications.

4. We note that in your method validation report for the analysis of you established a limit of NMT . Please include this limit in your finished product and stability specifications.

5. Please clarify the actual test dates for your accelerated stability data (p. 2052) and resubmit your stability data with the correct dates.

6. We acknowledge that you added a test for related substances in July 1998 and at the 6 and 9 months stations (lot #A980053) no related substance was detected We recommend that you reduce your limits for individual and total related substances because the current specifications are too broad compared to results obtained during your validation studies. Also, please specify on both your finished product and stability specifications, "Limit for individual related substances, excluding caprolactam."

7. Please submit updated room temperature stability data.

8. We note that you increased the upper limit of your hardness range from to accommodate your accelerated stability data for lot #B960222 . Room temperature hardness results for the same lot are from

s). Do you have an explanation for the high hardness values obtained during accelerated stability studies of lot #B960222 (p. 2052)?

9. Please include a test and specification for moisture in your stability specifications.

10. How did you calculate your expiration period?

11. Purified water and total weight should be included in Components/Composition statement. Please revise and resubmit.

B. In addition to responding to the deficiencies presented above, please include the primary function of each excipient in the component/composition statement.

Sincerely yours,

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

1. CHEMISTRY REVIEW # 1

2. ANDA # 75-602

3. NAME AND ADDRESS OF APPLICANT
Mikart, Incorporated
Attention: Cerie B. McDonald
1750 Chattahoochee Avenue, N.W.
Atlanta, GA 30318

4. LEGAL BASIS FOR ANDA SUBMISSION
The basis of this submission is the approved listed drug, Amicar® Tablets, 500 mg (NDA #15-197). There are no patent information and exclusivity period for the listed drug (pp 12, 14).

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Aminocaproic Acid

8. SUPPLEMENT PROVIDE FOR:
N/A

9. AMENDMENTS AND OTHER DATES:
March 17, 1999: Original Submission
April 28, 1999: Refuse to File
May 14, 1999: Amendment
May 17, 1999: Acceptable for Filing

10. PHARMACOLOGICAL CATEGORY
Antifibrinolytic Agent

11. ℞ or OTC
℞

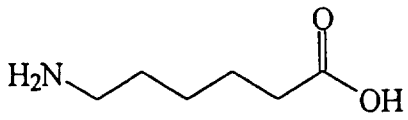
12. RELATED DMFs

13. DOSAGE FORM
Tablet

14. POTENCY
500 mg

15. CHEMICAL NAME AND STRUCTURE

Aminocaproic Acid. $C_6H_{13}NO_2$. 131.18. 6-Aminohexanoic acid



16. RECORDS AND REPORTS
N/A

17. COMMENTS
See review

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable, Major.

19. REVIEWER
Ijeoma N. Nnamani, Ph.D.

DATE COMPLETED
October 27, 1999

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10/22/99

1. CHEMISTRY REVIEW # 3

2. ANDA # 75-602

3. NAME AND ADDRESS OF APPLICANT
Mikart, Incorporated
Attention: Cerie B. McDonald
1750 Chattahoochee Avenue, N.W.
Atlanta, GA 30318

4. LEGAL BASIS FOR ANDA SUBMISSION
The basis of this submission is the approved listed drug, Amicar® Tablets, 500 mg (NDA #15-197). There are no patent information and exclusivity period for the listed drug (pp 12, 14).

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Aminocaproic Acid

8. SUPPLEMENT PROVIDE FOR:
N/A

9. AMENDMENTS AND OTHER DATES:
March 17, 1999: Original Submission
April 28, 1999: Refuse to File
May 14, 1999: Amendment
May 17, 1999: Acceptable for Filing
October 4, 1999: Bio Review #1
October 29, 1999: Chemistry Review #1
November 1, 1999: Labeling Review #1
March 21, 2000: Amendment
August 11, 2000: Labeling Review #2
August 11, 2000: Chemistry Review #2
September 5, 2000: Bioequivalence Audit by Div. Of Scientific Investigations
October 25, 2000: Amendment

10. PHARMACOLOGICAL CATEGORY
Antifibrinolytic Agent

11. Rx or OTC
Rx

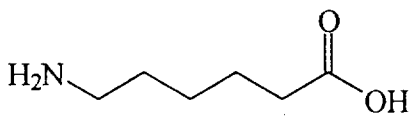
12. RELATED DMFs

13. DOSAGE FORM
Tablet

14. POTENCY
500 mg

15. CHEMICAL NAME AND STRUCTURE

Aminocaproic Acid. $C_6H_{13}NO_2$. 131.18. 6-Aminohexanoic acid



16. RECORDS AND REPORTS
N/A

17. COMMENTS
See review

18. CONCLUSIONS AND RECOMMENDATIONS
Approvable pending labeling and bioequivalence.

19. REVIEWER
Ijeoma N. Nnamani, Ph.D.

DATE COMPLETED
November 7, 2000

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Chem Rev #3

11/7/00