CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-811

CHEMISTRY REVIEW(S)

DEC 15 2000

38. Chemistry Comments to be Provided to the Applicant

DRUG PRODUCT: Mesna Injection, 100 mg/mL, 1 g in 10 mL Multidose Vial

The deficiency presented below represents a FAX deficiency.

A. Deficiency

duct

B. In addition to responding to the deficiency presented above, please note and acknowledge the following comments in your response:

1. Labeling deficiencies, if any, must also be addressed in your response.

2. A satisfactory compliance evaluation is needed for approval. We have requested an evaluation from the Office of Compliance.

3. We have requested an FDA laboratory to perform the Methods Validation. Please provide samples promptly when contacted. Please also provide a commitment to expeditiously resolve any deficiencies if the ANDA is approved before the study is completed.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

1. **CHEMISTRY REVIEW NO.** 3

2. **ANDA #** 75-811

3. **NAME AND ADDRESS OF APPLICANT**

American Pharmaceutical Partners, Inc.
2045 North Cornell Avenue
Melrose Park, IL 60160

4. **LEGAL BASIS FOR SUBMISSION**

Accepted by OGD

5. **SUPPLEMENT(s)**

N/A

6. **PROPRIETARY NAME**

N/A

7. **NONPROPRIETARY NAME**

Mesna

8. **SUPPLEMENT(s) PROVIDE(s) FOR:**

N/A

9. **AMENDMENTS AND OTHER DATES:**

February 25, 2000	Original Submission
November 13, 2000	Amendment (responding to deficiencies per chemistry review #1)
December 15, 2000	Amendment (SOP for NaCl assay in DS. The method was forwarded to the Lab for MV.)
January 3, 2001	New Correspondence (requesting a telecon to discuss the December 15, 2000 deficiency)
*January 23, 2001	Amendment (responding to deficiencies per chemistry review #2)

*subject of this review

10. **PHARMACOLOGICAL CATEGORY**

A detoxifying agent to inhibit the hemorrahagic cystitis induced by ifosfamide

11. **Rx or OTC**

Rx

12. **RELATED IND/NDA/DMF(s)**

als)
Vials)

13. **DOSAGE FORM**

Injection

14. **POTENCY**

100 mg/mL
1-g in a 10-mL Multiple Dose Vial

15. **CHEMICAL NAME AND STRUCTURE**

Sodium 2-Mercaptoethane Sulfonate

Molecular Formula: $C_2H_5NaO_3S_2$
Molecular Weight: 164.18

$[HSCH_2CH_2SO_3]^-Na^+$

16. **RECORDS AND REPORTS**

N/A

17. **COMMENTS**

The applicant noted and acknowledged the following as requested:

A. Labeling deficiencies, if any, must also be addressed in your response.

Response: Revised labeling and FPL were provided November 13, 2000. The December 15, 2000 Fax amendment did not provide additional comments.

B. A satisfactory compliance evaluation is needed for approval. We have requested an evaluation from the Office of Compliance.

Response: Noted and acknowledged.

C. We have requested an FDA laboratory to perform the Methods Validation. Please provide samples promptly when contacted. Please also provide a commitment to expeditiously resolve any deficiencies if the ANDA is approved before the study is completed.

Response: Samples were provided to the laboratory on December 21, 2000. APP commits to resolve any deficiencies if the ANDA is approved prior to completion of the study.

18. **CONCLUSIONS AND RECOMMENDATIONS**

Chemistry issues are closed.

Pending:

A. Satisfactory EER
B. Satisfactory MV

19. **REVIEWER:** Shirley S. Brown

DATE COMPLETED: 2/21/01

Shirley S. Brown January 29, 2001

2/21/01

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Contain Trade Secret, Commercial/Confidential Information and are not releasable.

Chem Rev # 3

1/29/01

SEP 1 2000

38. Chemistry Comments to be Provided to the Applicant

ANDA: 75-811 APPLICANT: American Pharmaceutical Partners, Inc.

DRUG PRODUCT: Mesna Injection, 100 mg/mL, 1 g in 10 mL Multidose Vial

The deficiencies presented below represent MAJOR deficiencies.

A. Deficiencies:

1. The European Pharmacopeia is not official in the United States. European Pharmacopeia changes in specification(s) or method(s) must be filed per the current United States requirements for changes to regulatory methods/limits. Please acknowledge.

2. Data qualifying the drug substance and impurity reference standards (structure, purity) or reference to the DMF where qualifying data may be found should be provided.

3. Regarding the manufacturing process:

(a)

ge
an

(b)

se

4.

or

5. Regarding the drug product release specifications:

   (a)

   (b)

   (c)

   (d)

6. Regarding the proposed commercial stability protocol: You propose to add one production lot annually stored inverted. The annual lot should also be tested upright (e.g. annually) until full term comparative data are available and upright testing is deleted with approval of a supplemental application.

7. The proposed stability specification for Benzyl Alcohol is --> Antimicrobial Effectiveness Testing data for the drug product supporting the effectiveness of the preservative at the level should be provided.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The microbiologist's review of the submission for sterility assurance is pending.

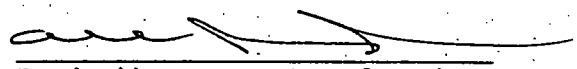
2. A satisfactory compliance evaluation of facilities referenced in the ANDA is required for approval. We have requested an evaluation from the Office of Compliance.

3. Your response must also address the labeling deficiencies.

4. Please provide any additional stability data that may be available.

5. The drug product is not listed in USP. Methods Validation will be requested following resolution of the testing issues.

Sincerely yours,



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