CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40278

CHEMISTRY REVIEW(S)

APPROVAL SUMMARY PACKAGE

ANDA NUMBER: 40-278 & 40-279

FIRM: American Pharmaceutical Partners, Inc. (APP)
(Transferred from Fujisawa USA, Inc.)

DOSAGE FORM: Injection

STRENGTH: 50 mg/mL
[ANDA 40-278: 50 mL and 100 mL vial; PBP]
[ANDA 40-279: 10 mL and 20 mL vial]

DRUG: Fluorouracil Injection USP

CGMP STATEMENT/EIR UPDATED STATUS:
EER is found acceptable as of 2-5-98 by M. Egas for the facilities 1 - 3 listed below for both ANDAs. *EER status for facility # 4 is pending.* This reviewer generated EER report on 9-14-98.

1. Fujisawa USA Inc.
2020 Ruby Street
Melrose Park, IL 60160
[Manufacturer finished drug product)

EER acceptable on 9/15/98
M Smela

BIO STUDY:
ANDA 40-278: Bio waiver is **acceptable** per review conducted by Gur J. P. Singh dated 2-6-98.

ANDA 40-279: Bio waiver is **acceptable** per review conducted by Gur J.P. Singh dated 2-11-98. A bio acceptance has been issued to the firm.

METHODS VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):

LABELING:
Satisfactory per review signed off for both ANDAs on 5-19-98.

STERILIZATION VALIDATION (IF APPLICABLE):

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.?):
Bio waiver is requested. No bio batch is manufactured for in vivo studies.

NDS Source: Referenced DMF is **adequate** per M. Shaikh's review dated 2-27-98 on review of 10-6-97 annual update to the DMF. No new information is submitted since last review.

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH WERE THEY MANUFACTURED VIA SAME PROCESS?)
ANDA 40-278:

APP submitted executed batch records (lot # 0197018A filled in a 100 mL vial; Batch size: L) and (lot # 0197018B filled in 50 mL vial; Batch size: L) for the Fluorouracil Injection USP 50 mg/mL.

ANDA 40-279:

APP submitted executed batch record for lot # 0197018 (Batch size: L) for the Fluorouracil Injection USP 50 mg/mL. The bulk solution is divided into two sublots: 0197018C (10 mL fill/10 mL vial) and 0197018D (20 mL/20 mL vial).

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?

ANDA 40-278:
Proposed intended production batch size: L

ANDA 40-279:
APP's proposed intended production batch size: L

Manufacturing process for intended production size batch is same as used for the stability batches.

cc: ANDAs 40-278 & 40-279
Division File
Field Copy

Endorsements:

HFD-625/M.Shaikh/9-14-98
HFD-625/M.Smela/9-15-98
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F/T by: bc/9-15-98

/S/ 9/22/98 /S/ M/C 9/23/98

Chem Closed

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 40-278
40-279

3. NAME AND ADDRESS OF APPLICANT
American Pharmaceuticals Partners, Inc. (APP)

Correspondence Address:
2045 North Cornell Avenue
Melrose Park, IL 60160

Corporate Address:
2825 Santa Monica Blvd
Santa Monica, CA 90404

NOTE:
Ownership of this ANDA has been transferred to American Pharmaceuticals Partners, Inc. (APP) from Fujisawa USA, IL per June 1, 1998 amendment. In amendment dated 4-30-98, Fujisawa clarified that it is their intention to market these products under APP after approval.

4. BASIS OF SUBMISSION
Listed drug product is ANDUCIL by Roche Laboratories approved in NDA # 12-209.

For information submitted in both ANDAs in support of this section: See CR # 1.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
None used

7. NONPROPRIETARY NAME
Fluorouracil Injection USP

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:
FIRM:
Original submission: 10-3-97 (Both ANDAs)
NC: 10-28-97 (ANDA 40-278)
MV Package: 11-24-97
FAX Amendment: 4-30-98 (Response to NA letter dated 3-31-98)
*Telephone Amendment: 5-13-98 (Labeling)
* NC: 6-1-98 (Change of ownership from Fujisawa)
* NC: 6-2-98 (Acceptance of ownership by American Pharmaceutical)
* NC: 6-3-98 (Intent to file fax amendment)

*Minor amendment: 7-16-98 (Response to May 28, 1998 Fax amendment).

FDA:
Accepted for filing: 10-6-97
Acknowledgment letters issued on: 11-27-97 (ANDA 40-279) and 11-10-97 (ANDA 40-278)
NA letter: 3-31-98
NA letter (Fax amendment): 5-28-98

10. PHARMACOLOGICAL CATEGORY
Antineoplastic

11. Rx or OTC
Rx

Treatment of carcinoma of colon, rectum, breast, stomach and pancreas

12. RELATED IND/NDA/DMF(s)
NDA 12-209...Roche
ANDA 40-023..Pharmacia & Upjohn..approved ANDA
DMF

DMF

DMF

DMF

DMF
DMF

13. DOSAGE FORM
Liquid

14. POTENCY
50 mg/mL

ANDA 40-278: 50 mL (2.5 g) and 100 mL (5.0 g) vials Pharmacy Bulk Package

ANDA 40-279: 10 mL and 20 mL vials

15. CHEMICAL NAME AND STRUCTURE
Listed in labeling insert per current USP

16. RECORDS AND REPORTS
N/A

17. COMMENTS
1. For consistency of this review with already approved ANDA 40-023, QA file has been checked for the proposed release and stability specifications in these ANDAs.
2. Referenced DMF adequate per review conducted by this reviewer on 2-27-98. No new information is submitted since last review.

3. Expiration dating period of 18 months is acceptable for both drug products listed in these ANDAs.
4. FPL: satisfactory
5. EER is incomplete for all the facilities listed in Section # 33 of this review.
6. Bio status: Acceptable for both ANDAs.
7. Micro review for APP's response in amendment dated 7-16-98 is pending.

18. CONCLUSIONS AND RECOMMENDATIONS
Chemistry Closed.

APP's response submitted in amendment dated 7-16-98 to micro deficiencies cited in 5-28-98 letter is pending review. The EER is also incomplete.

19. REVIEWER: Mujahid L. Shaikh
DATE COMPLETED: 7-28-98

cc: AND 40-278 & 40-279
DUP File
Division File
Field Copy

Endorsements:

HFD-625/M.Shaikh/7/28/98 /S/ 7/29/98
HFD-625/M.Smela/7/28/98
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F/T by: gp/7/28/98

/S/ 7/29/98

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information

Chemistry Review #3

Addendum to Chemist's Review # 3:

ANDA 40-278 & 40-279 (Fluorouracil Injection USP)

Chemistry Issues were previously closed per Review # 3.

Following updates need to be included in CR # 3.

1. Micro review became acceptable based on review dated 8-12-98 by P. Stinavage of ONDC.

2. EER status: Acceptable on 2-5-98 by M. Egas for facilities 1 - 3 as listed in section 33 of the CR # 3 as of report generated on 9-14-98. Status for facility # 4 listed in section # 33 of the CR # 3 is required and pending.

3. DMF status: No new information is submitted for the referenced DMF for Fluorouracil USP since last review completed on 2-27-98.

4. There is no change in USP monographs since completion of CR # 3.

Comment: Approved pending acceptable EER status for all the facilities listed in these ANDAs.

c.c: ANDA 40-278 & 40-279
Division File
FIELD COPY

Endorsements:

/S/ for MLS 9/15/98

HFD-625/M. Shaikh/9-14-98
HFD-625/M. Smela/9-15-98
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F/T by: bc/9-15-98

/S/ 9/23/98

EER is acceptable
by J.D. Ambrogio on 9/15/98
MJS