CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40266

CHEMISTRY REVIEW(S)

ANDA Number: 40-266

FIRM: Bigmar Inc.

DOSAGE FORM: Methotrexate for Injection USP.

STRENGTH 1 gram in a 50 mL vial.

CGMP STATEMENT/EER UPDATE STATEMENT:

EER pending. Acceptable 2/24/99 RW

BIO STUDY: Waiver granted 12/31/97

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

Not applicable. Both drug substance and drug product are USP.

STABILITY - ARE THE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION.

Yes. Container section describes a 50 mL clear glass vial with rubber cap and aluminum seal.

Tentative Expiration date is 24 months (2 years).

LABELING:

FPL found adequate on 12/9/98.

STERILIZATION VALIDATION (IF APPLICABLE):

Sterilization validation found adequate on 2/2/99.

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.)

No bio batch (waiver granted 12/31/97).

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH WERE THEY MANUFACTURED BY THE SAME PROCESS?)

One batch was manufactured at Liters.

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

Liters and Liters, (Both sizes will be manufactured in the same manner as stability batch).

/S/ 2/17/99

Prepared by Stephen Sherken on 2/11/99.

/S/ 2/18/99

1. CHEMISTRY REVIEW NO. 5

2. ANDA # 40-266

3. NAME AND ADDRESS OF APPLICANT

Bigmar Inc.
Johnstown, OH 43031-9141

4. LEGAL BASIS FOR SUBMISSION

505(j), 21 CFR 314.94

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Methotrexate for Injection USP, 1.000 g/vial

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

N/A

9. AMENDMENTS AND OTHER DATES:

DOA 7/31/97; Amend 9/17/97; Amend (Chemistry-Micro-Vol 2.1), 12/20/97; NA (Major-Chem) 2/9/98; Chem Amend 2/9/98; Major Chem-Label Amend 2/19/98; Micro Amend 5/29/98; Chem Amend 6/11/98; Micro NA 6/18/98; NA, Chem & Micro (FAX) 8/19/98; FAX Amend 9/18/98; NA FAX 10/23/98; Label Amend 10/28/98; Label Review 11/18/98; Amend 11/20/98; Micro Review 12/21/98; Label Amend 11/25/98; Label review for Approval 12/9/98; NA with Micro deficiencies (FAX) 12/24/98; NC (Micro) 1/19/99; NC (Micro) 1/27/99; Micro review for approval 2/2/99.

10. PHARMACOLOGICAL CATEGORY

Neoplastic Diseases

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

NDA 11-719, DMF-

13. DOSAGE FORM

Amorphous Caked Mass.

14. POTENCY

1 gm in a 50 mL vial.

15. CHEMICAL NAME AND STRUCTURE

Remains satisfactory (see review #1).

16. RECORDS AND REPORTS N/A

17. COMMENTS

No chemistry deficiencies remain.

Sterility assurance review on 2/2/99 of 1/19/99 and 1/27/99 amendments. No deficiencies found. Recommend approval.

Bio-waiver was granted in review dated 12/31/97.

EER from recommends withhold on 6/3/98. FUR pending.

Labeling review of 12/9/98 recommends approval.

18. CONCLUSIONS AND RECOMMENDATIONS

Approve ANDA 40-266 pending acceptable EER.

19. REVIEWER: DATE COMPLETED:

Stephen Sherken 2/11/99

cc: ANDA 40-266
Division File
Field Copy

Endorsements: 2/17/99

HFD-625/SSherken/2/9/99
HFD-625/Msmela/2/10/99 2/18/99
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Chemistry Review #5