

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
40265

MICROBIOLOGY REVIEW

OFFICE OF GENERIC DRUGS
Microbiologists Review #1
June 11, 1998

A. 1. ANDA: **40-265**

APPLICANT: Bigmar Inc.
9711 Sportsman Club Road
Johnstown, Ohio 43031-1941

2. PRODUCT NAME: **Methotrexate Injection, USP**
3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 25 mg/mL, 4 mL, 8 mL and 10 mL vial for IV, IA, IM and IT injection. Preservative Free Single Dose Vials.
4. METHOD(S) OF STERILIZATION:
5. PHARMACOLOGICAL CATEGORY: anti neoplastic

B. 1. DATE OF INITIAL SUBMISSION: **July 30, 1997. Subject of this Review.**

2. DATE OF AMENDMENT:
September 17, 1997. Subject of this Review.
December 20, 1997. Subject of this review.
February 9, 1998. Subject of this Review.

3. RELATED DOCUMENTS: DMFs not reviewed. 40-263 preserved and 40-266 lyophilized.

4. ASSIGNED FOR REVIEW: June 11, 1998.

C. REMARKS: A justification for processing is provided in the December 20, 1997 Amendment. Increases in impurities were seen after 121°C for 15 minutes. The 2 mL fill volume was dropped due to filling problems with filling this volume (page 1177).

D. CONCLUSIONS: The submission is not recommended for approval on the basis of sterility assurance. Specific comments are provided

ISI
James L. McVey *6/12/98*

initialed by R. Patel *received 8/11/98*

cc:

Original ANDA

Duplicate ANDA

Field Copy

drafted by: J. McVey

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OFFICE OF GENERIC DRUGS
Microbiologists Review #2
September 18, 1998

A. 1. ANDA: **40-265**

APPLICANT: Bigmar Inc.
9711 Sportsman Club Road
Johnstown, Ohio 43031-1941

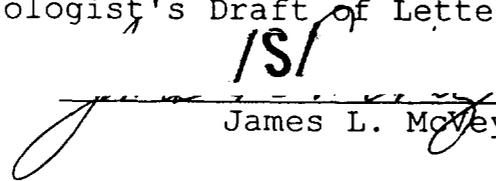
- 2. PRODUCT NAME: **Methotrexate Injection, USP**
- 3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 25 mg/mL, 2 mL, 4 mL, 8 mL and 10 mL vials for IV, IA and IM injection, non-preserved
- 4. METHOD(S) OF STERILIZATION:
- 5. PHARMACOLOGICAL CATEGORY: anti neoplastic

- B. 1. DATE OF INITIAL SUBMISSION: June 30, 1997.
- 2. DATE OF AMENDMENT:
September 17, 1997.
November 21, 1997.
February 16, 1998.
May 29, 1998. Subject of this review.
September 16, 1998. Subject of this Review.

- 3. RELATED DOCUMENTS: DMFs not reviewed.
- 4. ASSIGNED FOR REVIEW: September 18, 1998.

C. REMARKS: Reviewed with sister product 40-263, preserved. Deficiencies are the same and could be incorporated into one letter.

D. CONCLUSIONS: The submission is not recommended for approval on the basis of sterility assurance. Specific comments are provided in "Microbiologist's Draft of Letter to Applicant".

ISI

James L. McVey *9/18/98*

cc: initialed by R. Patel *Revised 9/18/98*

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Duplicate ANDA
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drafted by: J. McVey 40265na2.m

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microbiologist's review #2

OFFICE OF GENERIC DRUGS
Microbiologists Review #3
December 17, 1998

- A. 1. ANDA: **40-265**
- APPLICANT: Bigmar Inc.
9711 Sportsman Club Road
Johnstown, Ohio 43031-1941
2. PRODUCT NAME: **Methotrexate Injection, USP**
3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 25 mg/mL,
2 mL, 4 mL, 8 mL and 10 mL vials for IV, IA and IM
injection, non-preserved
4. METHOD(S) OF STERILIZATION:
5. PHARMACOLOGICAL CATEGORY: anti neoplastic
- B. 1. DATE OF INITIAL SUBMISSION: June 30, 1997.
2. DATE OF AMENDMENT:
September 17, 1997.
November 21, 1997.
February 16, 1998.
May 29, 1998.
September 16, 1998.
November 20, 1998. Subject of this Review.
3. RELATED DOCUMENTS: DMFs not reviewed.
4. ASSIGNED FOR REVIEW: December 17, 1998.
- C. REMARKS: Reviewed with sister product 40-263, preserved.
Deficiencies are the same and could be incorporated into
one letter. **A phone call is recommended to assure that
the deficiencies are understood.**
- D. CONCLUSIONS: The submission is not recommended for
approval on the basis of sterility assurance. Specific
comments are provided

JS *12/18/98*
James L. McVey
initialed by M. Fanning *MF 12/21/98*

cc:
Original ANDA
Duplicate ANDA
Field Copy
drafted by: J. McVey 40265na3.m

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Microbiologist's Review #3

OFFICE OF GENERIC DRUGS

Microbiologists Review #4

February 2, 1999

A. 1. ANDA: **40-265**

APPLICANT: Bigmar Inc.
9711 Sportsman Club Road
Johnstown, Ohio 43031-1941

2. PRODUCT NAME: **Methotrexate Injection, USP**
3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: 25 mg/mL, 2 mL, 4 mL, 8 mL and 10 mL vials for IV, IA and IM injection, non-preserved
4. METHOD(S) OF STERILIZATION:
5. PHARMACOLOGICAL CATEGORY: anti neoplastic

B. 1. DATE OF INITIAL SUBMISSION: June 30, 1997.

2. DATE OF AMENDMENT:
September 17, 1997.
November 21, 1997.
February 16, 1998.
May 29, 1998.
September 16, 1998.
November 20, 1998.

January 21, 1999 - Subject of this Review.

January 27, 1999 - Subject of this Review.

3. RELATED DOCUMENTS: DMFs not reviewed.
4. ASSIGNED FOR REVIEW: January 25, 1999.

C. REMARKS: Reviewed with sister product 40-263, preserved. Deficiencies are the same and could be incorporated into one letter.

D. CONCLUSIONS: The submission is recommended for approval on the basis of sterility assurance. Specific comments are provided in "Microbiologist's Draft of Letter to Applicant". *JS/*

2-2-99
James L. McVey

initialed by M. Fanning *MF*

cc:

Original ANDA
Duplicate ANDA
Field Copy

drafted by: J. McVey

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Microbiologist's Review #4