

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
40263

MICROBIOLOGY REVIEW

OFFICE OF GENERIC DRUGS

Microbiologists Review #1

June 10, 1998

A. 1. ANDA: **40-263**

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 and 10 mL vial for IV, IA and IM injection.
Preserved
- 4. METHOD(S) OF STERILIZATION:
- 5. PHARMACOLOGICAL CATEGORY: anti neoplastic

B. 1. DATE OF INITIAL SUBMISSION: ^{July Jan 6/11/98} June 30, 1997. Subject
of this Review.

- 2. DATE OF AMENDMENT:
September 17, 1997. Subject of this Review.
November 21, 1997. Subject of this review.
February 16, 1998. Subject of this Review.

- 3. RELATED DOCUMENTS: DMFs not reviewed.
- 4. ASSIGNED FOR REVIEW: May 27, 1998.

C. REMARKS: A justification for processing is provided in the November 21, 1997 Amendment. Increases in impurities were seen after 121 °C for 20 minutes. ✓

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

JS/

6/10/98
James L. McVey

initialed by R. Patel *REC: rpl 6/10/98*

cc:

Original ANDA
Duplicate ANDA
Field Copy

drafted by: J. McVey 40263na1.m

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microbiologist Review #1

OFFICE OF GENERIC DRUGS
Microbiologists Review #2
September 17, 1998

- A. 1. ANDA: **40-263**
- 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 and 10 mL vial for IV, IA and IM injection.
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 05, 1998. Subject of this Review.
3. RELATED DOCUMENTS: DMFs not reviewed.
4. ASSIGNED FOR REVIEW: September 16, 1998.
- C. REMARKS: Reviewed with sister, non preserved products ,
40-265. Same deficiencies for both ANDAs.
- D. CONCLUSIONS: The submission is not recommended for
approval on the basis of sterility assurance. Specific
comments are provided


James L. McVey *9/19/98*

initialed by R. Patel *Patel 9/14/98*

cc:

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drafted by: J. McVey 40263na2.m

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Microbiology Review #2

OFFICE OF GENERIC DRUGS

Microbiologists Review #3

December 17, 1998

A. 1. ANDA: **40-263**

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 and 10 mL vial for IV, IA and IM injection.
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 5, 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, non preserved products ,
40-265. Same deficiencies for both ANDAs. **A phone call
is recommended to make sure they understand these
deficiencies.**

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

ISI

James L. McVey *12/17/98*

initialed by: M. Fanning *M.F. 12/11/98*

cc:

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Duplicate ANDA
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drafted by: J. McVey 40263na3.m

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microbiologist Review #3

OFFICE OF GENERIC DRUGS
Microbiologists Review #4
February 2, 1999

A. 1. ANDA: **40-263**

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 and 10 mL vials for IV, IA and IM injection,
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 5, 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 40-265, non-
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.

JS
James L. McVey *2-2-99*

cc:

initialed by M. Fanning *MZ* *2/2/99*
Original ANDA
Duplicate ANDA
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drafted by: J. McVey 40263a4.m

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Microbiologists Review #4