

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-915**

**CHEMISTRY REVIEW(S)**

# **NDA 21-915**

**Ondansetron Injection, USP in PL2408 Plastic Container**

**(8 mg/50 mL and 32 mg/50 mL)**

**Baxter Healthcare Corporation**

**Marie Kowblansky, Ph.D.**  
**DIVISION OF GASTROINTESTINAL AND COAGULATION**  
**DRUG PRODUCTS**

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## Chemistry Review Data Sheet

## Chemistry Review Data Sheet

1. NDA 21-915
2. REVIEW #: 1
3. REVIEW DATE: 11/15/05
4. REVIEWER: Marie Kowblansky, PhD
5. PREVIOUS DOCUMENTS: None
6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed  
 Original  
 Amendment

Document Date  
 April 11, 2005  
 December 12, 2005

## 7. NAME &amp; ADDRESS OF APPLICANT:

Name: Baxter Healthcare Corporation  
 Address: 1620 Waukegan Road  
 McGaw Park, Illinois 60085  
 Representative: Vicki Drews  
 Telephone: 847-473-6296

## 8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Ondansetron Injection, USP
- b) Non-Proprietary Name (USAN): ondansetron hydrochloride
- c) Code Name/# (ONDC only):
- d) Chem. Type/Submission Priority (ONDC only):
  - Chem. Type: 3
  - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b)(2) with ZOFTRAN® Injection (NDA 20-007) being the reference drug product.

10. PHARMACOL. CATEGORY: antiemetic, prevention of nausea and vomiting associated with emetogenic cancer chemotherapy

11. DOSAGE FORM: injection

12. STRENGTH/POTENCY: 8 mg/50 mL and 32 mg/50 mL

13. ROUTE OF ADMINISTRATION: intravenous

14. Rx/OTC DISPENSED:  Rx  OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

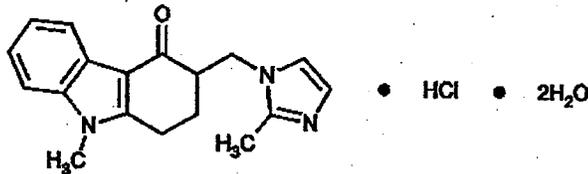
SPOTS product – Form Completed  
 Not a SPOTS product

Chemistry Review Data Sheet

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

**CHEMICAL NAME:** 4*H*-Carbazol-4-one, 1,2,3,9-tetrahydro-9-methyl-3-(2-methyl-1*H*-imidazol-1-yl)methyl-, monohydrochloride, (±)-, dihydrate.

**STRUCTURE:**



**MOLECULAR FORMULA:** C<sub>18</sub>H<sub>19</sub>N<sub>3</sub>O·HCl·2H<sub>2</sub>O  
**MOLECULAR WEIGHT:** 365.86

17. RELATED/SUPPORTING DOCUMENTS:

**A. DMFs:**

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE <sup>1</sup>	STATUS <sup>2</sup>	DATE REVIEW COMPLETED	COMMENTS
—	2	—	Ondansetron hydrochloride	3	Adequate	6/1/2005	Reviewer S.Basaran, OGD
11,691	3	Baxter	Terminal sterilization in PL 2408 containers		Under review	--	Under review by Microbiology Staff
11,691	3	Baxter	PL 2408 containers	4	---	---	---

<sup>1</sup> Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

<sup>2</sup> Adequate, Inadequate, or N/A (enough data in the application, therefore the DMF did not need to be reviewed)

**B. Other Documents:**

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	20-007	Zofran Injection

## Chemistry Review Data Sheet

## 18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics		12/16/05	Wen Jen Chen
EES	Inspection requested		pending
Pharm/Tox	Approval	11/9/05	Ke Zhang
Biopharm	pending		
Methods Validation	Not required	----	----
EA*	Not required	10/18/2005	Marie Kowblansky
Microbiology	Approvable	12/21/05	Stephen E. Langille

\*Per 21CFR 25.31(a) the applicant appropriately claims categorical exclusion on the basis that there will be no increase in use of the active moiety.

APPEARS THIS WAY  
ON ORIGINAL

## Executive Summary Section

## Chemistry Review for NDA 21-915

The Executive Summary

## I. Recommendations

A. **Recommendation and Conclusion on Approvability** -- from the CMC perspective, both proposed strengths may be approved with a 24-month expiration date (with room temperature storage), pending

- satisfactory resolution of the deficiencies cited in the Microbiology review
- a recommendation from the Office of Compliance that the manufacturing facilities are Acceptable.

B. **Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable** – None required

## II. Summary of Chemistry Assessments

## A. Description of the Drug Product(s) and Drug Substance(s)

Ondansetron Injection is a sterile iso-osmotic, single-use parenteral injection product, requiring no further dilution prior to administration. The active drug substance in the formulation is ondansetron hydrochloride, USP, which will conform to all recently upgraded USP requirements. The product will be manufactured at two strengths, 8 mg and 32 mg of ondansetron (as ondansetron hydrochloride) per 50 mL of 0.9% aqueous sodium chloride solution that is maintained at pH 3.5 with citrate buffer. All formulation excipients are commonly used in injectable formulations and will conform to USP requirements. Their compatibility in the current formulation is demonstrated. Baxter dual ported 50 mL PL 2408 flexible plastic container with foil overwrap will be used for packaging the product.

Terminal sterilization will be performed in the flexible plastic container in which the product will be marketed. Data are provided to demonstrate that both the product and plastic container remain stable under the sterilization conditions. Additional studies evaluating the compatibility of the product with the plastic container showed that even after six months at 40°C, no significant changes were noted in any of the solutions.

Stability studies conducted at 25°C and at 40°C demonstrate that both the drug substance and formulated product are remarkably stable. There are no trends indicative of instability in the drug product, even after six months of storage at accelerated conditions; none of the test results depart from their initial values. The stability studies justify the proposed 24-month expiration.

Although both proposed strengths may be approved from a CMC perspective, a decision has been made by HFD-180 that the 8mg/50mL product should not be approved, based on other than CMC considerations.

## Executive Summary Section

### B. Description of How the Drug Product is Intended to be Used

The product is meant for intravenous injection for the prevention of nausea and vomiting induced by emetogenic chemotherapy and post-operative nausea and vomiting. The recommended dosing is either as a single 32 mg dose infused over 15 minutes or as three 0.15 mg/kg doses.

### C. Basis for Approvability or Not-Approval Recommendation

The drug substance conforms to USP requirements and the manufacturing process for the drug product is well controlled with acceptable specifications. The packaging is appropriate for the product.

## III. Administrative

### A. Reviewer's Signature

### B. Endorsement Block

ChemistName/Date: Marie Kowblansky, PhD  
BranchChief ONDQA/Date: Moo Jhong Rhee, PhD  
DivisionDirector ONDQA/Date Elaine Morefield, PhD  
ProjectManagerName/Date: Betsy Scroggs, Pharm.D

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ON ORIGINAL**

16 Page(s) Withheld

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       § 552(b)(4) Draft Labeling

       § 552(b)(5) Deliberative Process

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/s/

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Marie Kowblansky  
12/23/2005 01:14:41 PM  
CHEMIST

Elaine Morefield  
12/23/2005 01:38:24 PM  
CHEMIST

**NDA 21-915****Ondansetron Injection, USP in PL2408 Plastic Container****(8 mg/50 mL and 32 mg/50 mL)****Baxter Healthcare Corporation****Marie Kowblansky, Ph.D.  
DIVISION OF GASTROINTESTINAL AND COAGULATION  
DRUG PRODUCTS**

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B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable – None required.....	6
<b>II. Summary of Chemistry Assessments .....</b>	<b>6</b>
A. Description of the Drug Product(s) and Drug Substance(s).....	6
B. Description of How the Drug Product is Intended to be Used .....	6
C. Basis for Approvability or Not-Approval Recommendation.....	7
<b>III. Administrative.....</b>	<b>7</b>
A. Reviewer's Signature .....	7
B. Endorsement Block .....	7
<b>Chemistry Assessment.....</b>	<b>8</b>

## Chemistry Review Data Sheet

## Chemistry Review Data Sheet

1. NDA 21-915
2. REVIEW #: 2
3. REVIEW DATE: 1/25/06
4. REVIEWER: Marie Kowblansky, PhD
5. PREVIOUS DOCUMENTS: Review #1
6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed  
Original  
Amendment

Document Date  
April 11, 2005  
December 12, 2005

## 7. NAME &amp; ADDRESS OF APPLICANT:

Name: Baxter Healthcare Corporation  
Address: 1620 Waukegan Road  
McGaw Park, Illinois 60085  
Representative: Vicki Drews  
Telephone: 847-473-6296

## 8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Ondansetron Injection, USP
- b) Non-Proprietary Name (USAN): ondansetron hydrochloride
- c) Code Name/# (ONDC only):
- d) Chem. Type/Submission Priority (ONDC only):
  - Chem. Type: 3
  - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b)(2) with ZOFTRAN® Injection (NDA 20-007) being the reference drug product.

10. PHARMACOL. CATEGORY: antiemetic, prevention of nausea and vomiting associated with emetogenic cancer chemotherapy

11. DOSAGE FORM: injection

12. STRENGTH/POTENCY: 8 mg/50 mL and 32 mg/50 mL

13. ROUTE OF ADMINISTRATION: intravenous

14. Rx/OTC DISPENSED:  Rx  OTC

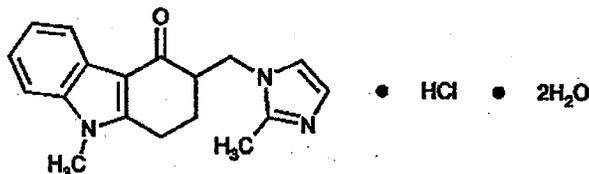
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed  
 Not a SPOTS product

## Chemistry Review Data Sheet

## 16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

**CHEMICAL NAME:** 4*H*-Carbazol-4-one, 1,2,3,9-tetrahydro-9-methyl-3-(2-methyl-1*H*-imidazol-1-yl)methyl-, monohydrochloride, (±)-, dihydrate.

**STRUCTURE:**

**MOLECULAR FORMULA:** C<sub>18</sub>H<sub>19</sub>N<sub>3</sub>O·HCl·2H<sub>2</sub>O

**MOLECULAR WEIGHT:** 365.86

## 17. RELATED/SUPPORTING DOCUMENTS:

**A. DMFs:**

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE <sup>1</sup>	STATUS <sup>2</sup>	DATE REVIEW COMPLETED	COMMENTS
—	2	—	Ondansetron hydrochloride	3	Adequate	6/1/2005	Reviewer S.Basaran, OGD
11,691	3	Baxter	Terminal sterilization in PL 2408 containers		Adequate	1/17/06	Stephen E. Langille
11,691	3	Baxter	PL 2408 containers	4	---	---	---

<sup>1</sup> Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

<sup>2</sup> Adequate, Inadequate, or N/A (enough data in the application, therefore the DMF did not need to be reviewed)

**B. Other Documents:**

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	20-007	Zofran Injection

## Chemistry Review Data Sheet

## 18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	Approval of 32 mg only Approvable for 8 mg, pending submission of additional data	12/16/05	Wen Jen Chen
EES*	Acceptable	12/30/06	OC
Pharm/Tox	Approval	11/9/05	Ke Zhang
Biopharm	Biowaiver	1/5/06	Suliman Alfayoumi
Methods Validation	Not required	----	----
EA**	Not required	10/18/2005	Marie Kowblansky
Microbiology	Approval	1/24/06	Stephen E. Langille

\* EES report appended to this review

\*\* Per 21CFR 25.31(a) the applicant appropriately claims categorical exclusion on the basis that there will be no increase in use of the active moiety.

**APPEARS THIS WAY  
ON ORIGINAL**

## Executive Summary Section

## Chemistry Review for NDA 21-915

The Executive Summary**I. Recommendations**

- A. Recommendation and Conclusion on Approvability** -- from the CMC perspective, both proposed strengths (8 mg/mL and 32 mg/mL) may be approved with a 24-month expiration date and room temperature storage, pending resolution of the two labeling issues listed at the conclusion of this review.
- B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable** – None required

**II. Summary of Chemistry Assessments****A. Description of the Drug Product(s) and Drug Substance(s)**

Ondansetron Injection is a sterile iso-osmotic, single-use parenteral injection product, requiring no further dilution prior to administration. The active drug substance in the formulation is ondansetron hydrochloride, USP, which will conform to all recently upgraded USP requirements. The product will be manufactured to contain either 8 mg or 32 mg of ondansetron (as ondansetron hydrochloride) per 50 mL of 0.9% aqueous sodium chloride solution that is maintained at pH 3.5 with citrate buffer. All formulation excipients are commonly used in injectable formulations and will conform to USP requirements. Their compatibility in the current formulation is demonstrated. Baxter dual ported 50 mL PL 2408 flexible plastic container with foil overwrap will be used for packaging the product.

Terminal sterilization will be performed in the flexible plastic container in which the product will be marketed. Data are provided to demonstrate that both the product and plastic container remain stable under the sterilization conditions. Additional studies evaluating the compatibility of the product with the plastic container showed that even after six months at 5°C or 40°C, no significant changes were noted in any of the solutions.

Stability studies conducted at 25°C and at 40°C demonstrate that both the drug substance and formulated product are remarkably stable. There are no trends indicative of instability in the drug product, even after six months of storage at accelerated conditions; none of the test results depart from their initial values. The stability studies justify the proposed 24-month expiration with storage at 25°C.

Although both proposed strengths may be approved from a CMC perspective (once labeling issues are resolved), a decision has been made by HFD-180 that the 8mg/50mL product could not be approved at the present time, based on other than CMC considerations.

**B. Description of How the Drug Product is Intended to be Used**

This product is intended for use in the prevention of nausea and vomiting induced by emetogenic chemotherapy. It is administered by intravenous injection, with recommended dosing being either as a single 32 mg dose infused over 15 minutes or as three 0.15 mg/kg doses.

## Executive Summary Section

### C. Basis for Approvability or Not-Approval Recommendation

The drug substance conforms to USP requirements and the manufacturing process for the drug product is well controlled with acceptable specifications for the finished product.

### III. Administrative

#### A. Reviewer's Signature

#### B. Endorsement Block

ChemistName/Date: Marie Kowblansky, PhD  
BranchChief ONDQA/Date: Moo Jhong Rhee, PhD  
ProjectManagerName/Date: Betsy Scroggs, Pharm.D

**APPEARS THIS WAY  
ON ORIGINAL**

4 Page(s) Withheld

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       § 552(b)(4) Draft Labeling

       § 552(b)(5) Deliberative Process

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this page is the manifestation of the electronic signature.**  
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/s/

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Marie Kowblansky  
1/26/2006 12:04:00 PM  
CHEMIST

Moo-Jhong Rhee  
1/26/2006 12:11:18 PM  
CHEMIST  
Chief, Branch III

**NDA 21-915**

**Ondansetron Injection, USP in PL2408 Plastic Container**

**(32 mg/50 mL)**

**Baxter Healthcare Corporation**

**Marie Kowblansky, Ph.D.**  
**Pre-Marketing Assessment Division II, Branch III, ONDQA**  
**for**  
**DIVISION OF GASTROINTESTINAL PRODUCTS**

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B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable – None required .....	6
<b>II. Summary of Chemistry Assessments .....</b>	<b>6</b>
A. Description of the Drug Product(s) and Drug Substance(s).....	6
B. Description of How the Drug Product is Intended to be Used .....	6
C. Basis for Approvability or Not-Approval Recommendation.....	6
<b>III. Administrative.....</b>	<b>7</b>
A. Reviewer's Signature .....	7
B. Endorsement Block .....	7
<b>Chemistry Assessment .....</b>	<b>7</b>

## Chemistry Review Data Sheet

## Chemistry Review Data Sheet

1. NDA 21-915
2. REVIEW #: 3
3. REVIEW DATE: 4/26/06
4. REVIEWER: Marie Kowblansky, PhD
5. PREVIOUS DOCUMENTS: Review #1 and #2
6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original	April 11, 2005
Amendment	December 12, 2005
Amendment	April 3, 2006
Amendment	April 14, 2006

## 7. NAME &amp; ADDRESS OF APPLICANT:

Name: Baxter Healthcare Corporation  
 Address: 1620 Waukegan Road  
 McGaw Park, Illinois 60085  
 Representative: Vicki Drews  
 Telephone: 847-473-6296

## 8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Ondansetron Injection, USP
- b) Non-Proprietary Name (USAN): ondansetron hydrochloride
- c) Code Name/# (ONDC only):
- d) Chem. Type/Submission Priority (ONDC only):
  - Chem. Type: 3
  - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b)(2) with ZOFTRAN® Injection (NDA 20-007) being the reference drug product.

10. PHARMACOL. CATEGORY: antiemetic, prevention of nausea and vomiting associated with emetogenic cancer chemotherapy

11. DOSAGE FORM: injection

12. STRENGTH/POTENCY: 32 mg/50 mL

13. ROUTE OF ADMINISTRATION: intravenous

14. Rx/OTC DISPENSED:  Rx  OTC

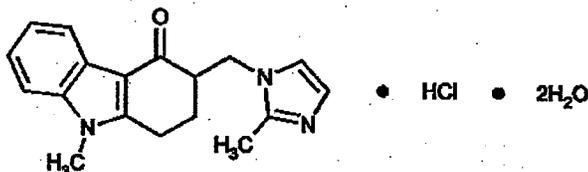
## Chemistry Review Data Sheet

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

\_\_\_\_\_ SPOTS product – Form Completed  
 Not a SPOTS product

## 16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

**CHEMICAL NAME:** 4*H*-Carbazol-4-one, 1,2,3,9-tetrahydro-9-methyl-3-(2-methyl-1*H*-imidazol-1-yl)methyl-, monohydrochloride, (±)-, dihydrate.

**STRUCTURE:**

**MOLECULAR FORMULA:** C<sub>18</sub>H<sub>19</sub>N<sub>3</sub>O·HCl·2H<sub>2</sub>O  
**MOLECULAR WEIGHT:** 365.86

## 17. RELATED/SUPPORTING DOCUMENTS:

**A. DMFs:**

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE <sup>1</sup>	STATUS <sup>2</sup>	DATE REVIEW COMPLETED	COMMENTS
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11,691	3	Baxter	Terminal sterilization in PL 2408 containers		Adequate	1/17/06	Stephen E. Langille
11,691	3	Baxter	PL 2408 containers	4	---	---	---

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Other codes indicate why the DMF was not reviewed, as follows:

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3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

<sup>2</sup> Adequate, Inadequate, or N/A (enough data in the application, therefore the DMF did not need to be reviewed)

## Chemistry Review Data Sheet

## B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	20-007	Zofran Injection

## 18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	Approval of 32 mg only Approvable for 8 mg, pending submission of additional data	12/16/05	Wen Jen Chen
EES*	Acceptable	12/30/06	OC
Pharm/Tox	Approval	11/9/05	Ke Zhang
Biopharm	Biowaiver	1/5/06	Suliman Alfayoumi
Methods Validation	Not required	----	----
EA**	Not required	10/18/2005	Marie Kowblansky
Microbiology	Approval	1/24/06	Stephen E. Langille

\* EES report appended to this review

\*\* Per 21CFR 25.31 (a) the applicant appropriately claims categorical exclusion on the basis that there will be no increase in use of the active moiety.

**APPEARS THIS WAY  
ON ORIGINAL**

## Executive Summary Section

## Chemistry Review for NDA 21-915

The Executive Summary**I. Recommendations**

- A. **Recommendation and Conclusion on Approvability** -- from the CMC perspective, the product may be approved with a 24-month expiration date.
- B. **Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable** – None required

**II. Summary of Chemistry Assessments****A. Description of the Drug Product(s) and Drug Substance(s)**

Ondansetron Injection is a sterile iso-osmotic, single-use parenteral injection product, requiring no further dilution prior to administration. The active drug substance in the formulation is ondansetron hydrochloride, USP, which will conform to all recently upgraded USP requirements. The product will be manufactured to contain 32 mg of ondansetron (as ondansetron hydrochloride) per 50 mL of 0.9% aqueous sodium chloride solution that is maintained at pH 3.5 with citrate buffer. All formulation excipients are commonly used in injectable formulations and will conform to USP requirements. Their compatibility in the current formulation is demonstrated. Baxter dual ported 50 mL PL 2408 flexible plastic container with foil overwrap will be used for packaging the product.

Terminal sterilization will be performed in the flexible plastic container in which the product will be marketed. Data are provided to demonstrate that both the product and plastic container remain stable under the sterilization conditions. Additional studies evaluating the compatibility of the product with the plastic container showed that even after six months at 5°C or 40°C, no significant changes were noted in any of the solutions.

Stability studies conducted at 25°C and at 40°C demonstrate that both the drug substance and formulated product are remarkably stable. There are no trends indicative of instability in the drug product, even after six months of storage at accelerated conditions; none of the test results depart from their initial values. The stability studies justify the proposed 24-month expiration.

The original submission included two strengths for this product, 8 mg/50 mL and 32 mg/ 50 mL. Although both proposed strengths were found acceptable for approval from a CMC perspective, the 8 mg dose was withdrawn in the April 3, 2006 submission

**B. Description of How the Drug Product is Intended to be Used**

This product is intended for use in the prevention of nausea and vomiting induced by emetogenic chemotherapy. It is administered by intravenous injection.

**C. Basis for Approvability or Not-Approval Recommendation**

The drug substance conforms to USP requirements and the manufacturing process for the drug product is well controlled with acceptable specifications for the finished product.

2 Page(s) Withheld

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       § 552(b)(4) Draft Labeling

       § 552(b)(5) Deliberative Process

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/s/

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Marie Kowblansky  
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CHEMIST

Moo-Jhong Rhee  
5/1/2006 10:37:30 AM  
CHEMIST  
Chief, Branch III

**MEMO TO FILE**

**To:** NDA 21-915 (Ondansetron Injection)  
**From:** Marie Kowblansky, PhD  
**Through:** Moo-Jhong Rhee, PhD, Branch Chief, ONDQA  
**Date:** 12/20/06  
**Subject:** Amendment dated October 26, 2006

On May 1, 2006 ONDQA completed its review of NDA 21-915, with a recommendation for Approval of the application. However, the Agency's letter of May 26, 2006, informed the firm that final approval of the application could not be made effective until December 24, 2006, the expiration date for marketing exclusivity for the reference listed product. Baxter resubmitted their request for final approval on October 26, 2006, submitting

1) Minor clarification regarding Microbiology issues. This information was forwarded to the Microbiology Review Staff, who decided that the submitted information was acceptable and no further action was indicated

2) Updated labeling. There are no CMC revisions to either the package insert or container labeling compared to what was evaluated and found acceptable in the original review of this application.

The original inspection requests included a request for inspection of the Baxter Albonito facility (CFN 2649614). On December 19, 2006, C. Cruz of the Office of Compliance notified us that an inspection of that facility was not required because only packaging assembly (with no product filling) was conducted there. We were requested by OC to rescind our inspection request for the facility. With the deletion of the facility from the inspection list, the Office of Compliance issued an overall recommendation of Acceptable for all manufacturing facilities covered in this NDA. (See appended report.)

Therefore, the recommendation from ONDQA is that the NDA should be approved.

**APPEARS THIS WAY  
ON ORIGINAL**

1 Page(s) Withheld

X § 552(b)(4) Trade Secret / Confidential

       § 552(b)(4) Draft Labeling

       § 552(b)(5) Deliberative Process

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/s/

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12/20/2006 01:01:57 PM  
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