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RESEARCH**

*APPLICATION NUMBER:*

**21-915**

**CLINICAL PHARMACOLOGY AND  
BIOPHARMACEUTICS REVIEW(S)**

**MEMORANDUM**

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**DATE:** 1/5/06

**FROM:** Suliman I. Al-Fayoumi, Ph.D., Clinical Pharmacology and Biopharmaceutics Reviewer, Division of Clinical Pharmacology 3, Office of Clinical Pharmacology & Biopharmaceutics

**TO:** File of New Drug Application 21-915

**THROUGH:** Brian Harvey, M.D., Ph.D., Director, Division of Gastroenterology Products

**SUBJECT:** Biowaiver Request

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This memorandum addresses the request for a biowaiver for ondansetron injection, 32 mg submitted under NDA 21-915.

A waiver of the requirements for evidence of *in vivo* bioavailability for ondansetron premixed injection has been requested by the sponsor per 21 CFR 320.22(b)(1). The proposed product is a true solution which is intended for intravenous administration. In addition, the proposed product contains the same active and inactive ingredients as those of the current reference listed drug (Zofran<sup>®</sup> Injection).

In accordance with 21 CFR 320.22(b)(1), the sponsor's request of waiver of the requirements for evidence of *in vivo* bioavailability for ondansetron premixed injection, 32 mg is granted.

**APPEARS THIS WAY  
ON ORIGINAL**

**APPEARS THIS WAY  
ON ORIGINAL**

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/s/

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Suliman Alfayoumi  
1/17/2006 10:12:26 AM  
BIOPHARMACEUTICS

Dennis Bashaw  
1/17/2006 11:33:22 AM  
BIOPHARMACEUTICS

<b>DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION</b>		<b>Clinical Pharmacology (HFD 870) Tracking/Action Sheet for Formal/Informal Consults</b>		
From: Tien-Mien Chen, Ph.D. (HFD-870)			To: <b>DOCUMENT ROOM (LOG-IN and LOG-OUT)</b> Please log-in this consult and review action for the specified IND/NDA submission	
DATE: 12/18/06	IND No.: Serial No.:	NDA No. 21-915	DATE OF DOCUMENT 03/27/06, 10/27/06	
NAME OF DRUG [Ondansetron Inj., USP]	PRIORITY CONSIDERATION		Date of informal/Formal Consult: 04/11/06	
NAME OF THE SPONSOR: [Baxter]				
<b>TYPE OF SUBMISSION</b>				
<b>CLINICAL PHARMACOLOGY/BIOPHARMACEUTICS RELATED ISSUE</b>				
<input type="checkbox"/> PRE-IND	<input type="checkbox"/> DISSOLUTION/IN-VITRO RELEASE	<input type="checkbox"/> FINAL PRINTED LABELING		
<input type="checkbox"/> ANIMAL to HUMAN SCALING	<input type="checkbox"/> BIOAVAILABILITY STUDIES	<input checked="" type="checkbox"/> LABELING REVISION		
<input type="checkbox"/> IN-VITRO METABOLISM	<input type="checkbox"/> IN-VIVO WAIVER REQUEST	<input type="checkbox"/> CORRESPONDENCE		
<input type="checkbox"/> PROTOCOL	<input type="checkbox"/> SUPAC RELATED	<input type="checkbox"/> DRUG ADVERTISING		
<input type="checkbox"/> PHASE II PROTOCOL	<input type="checkbox"/> CMC RELATED	<input type="checkbox"/> ADVERSE REACTION REPORT		
<input type="checkbox"/> PHASE III PROTOCOL	<input type="checkbox"/> PROGRESS REPORT	<input type="checkbox"/> ANNUAL REPORTS		
<input type="checkbox"/> DOSING REGIMEN CONSULT	<input type="checkbox"/> SCIENTIFIC INVESTIGATIONS	<input type="checkbox"/> FAX SUBMISSION		
<input type="checkbox"/> PK/PD- POPPK ISSUES	<input type="checkbox"/> MEETING PACKAGE (EOP2/Pre-NDA/CMC/Pharmacometrics/Others)	<input type="checkbox"/> OTHER (SPECIFY BELOW): [     ]		
<input type="checkbox"/> PHASE IV RELATED				
<b>REVIEW ACTION</b>				
<input type="checkbox"/> NAI (No action indicated)	<input type="checkbox"/> Oral communication with Name: [     ]	<input type="checkbox"/> Formal Review/Memo (attached)		
<input type="checkbox"/> E-mail comments to:	<input type="checkbox"/> Comments communicated in meeting/Telecon. see meeting minutes dated: [     ]	<input checked="" type="checkbox"/> See comments below		
<input type="checkbox"/> Medical <input type="checkbox"/> Chemist <input type="checkbox"/> Pharm-Tox		<input type="checkbox"/> See submission cover letter		
<input type="checkbox"/> Micro <input type="checkbox"/> Pharmacometrics <input type="checkbox"/> Others (Check as appropriate and attach e-mail)		<input type="checkbox"/> OTHER (SPECIFY BELOW): [     ]		
<b>REVIEW COMMENT(S)</b>				
<input checked="" type="checkbox"/> <b>NEED NOT BE COMMUNICATED TO THE SPONSOR</b>		<input type="checkbox"/> <b>HAVE BEEN COMMUNICATED TO THE SPONSOR</b>		
<b>COMMENTS/SPECIAL INSTRUCTIONS:</b> [X] On 03/30/05, Baxter submitted a 505(b)(2) application for Ondansetron Injection, USP in PL 2408 plastic container seeking approval for Ondansetron Injection, a premix in IntraVia Plastic Container, 8 mg/50 mL and 32 mg/50 mL. Zofran (ondansetron) Injectable Injection (32 mg/50 mL) in plastic container is the currently approved brand name from GSK (the innovator). During discussions between the Agency and Baxter prior to its NDA's PDUFA goal date, the sponsor agreed to remove the lower strength of 8 mg/50 mL for which the Agency had concerns on its efficacy. NDA 21-915 was deemed "Approvable". On 03/27/06 and 10/27/06, Baxter submitted their responses to the Approvable letter to withdraw the lower strength (8 mg/50 ml in plastic container). No changes were made to the "Pharmacokinetics" subsection under Clinical Pharmacology section of the labeling.				
<b>Recommendation:</b> (Need not be sent to the sponsor): The sponsor submitted their responses to Agency's concerns and decided to remove the lower strength, 8 mg/mL, with no changes to the Clinical Pharmacology section. The sponsor's responses are acceptable from Office of Clinical Pharmacology perspective.				
SIGNATURE OF REVIEWER: <u>Tien-Mien Chen, Ph.D.</u>			Date <u>12/18/06</u>	
SIGNATURE OF ACTING TEAM LEADER: <u>T. Ghosh, Ph.D.</u>			Date <u>12/18/06</u>	
CC.: HFD # [180]; TL: [TG]			Project Manager: <u>G. Randazzo</u> Date <u>12/18/06</u>	

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/s/

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Tien-Mien Chen  
12/21/2006 09:09:44 AM  
BIOPHARMACEUTICS

Tapash Ghosh  
12/21/2006 12:34:55 PM  
BIOPHARMACEUTICS