

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

203050Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

EXCLUSIVITY SUMMARY

NDA # 203050

SUPPL #

HFD # 180

Trade Name

Generic Name Palonosetron Hydrochloride

Applicant Name Dr. Reddy's Laboratories Limited

Approval Date, If Known November 2, 2012

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒

NO ☐

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(2)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES ☐

NO ☒

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

N/A

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

N/A

d) Did the applicant request exclusivity?

YES ☐ NO ☒

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES ☐ NO ☒

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES ☐ NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES ☒ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 021372 Aloxi (palonosetron hydrochloride) injection

NDA# 022233 Aloxi (palonosetron hydrochloride) capsule

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES ☐ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a)

is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES ☐ NO ☒

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES ☐ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES ☐ NO ☐

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES ☐ NO ☐

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES ☐ NO ☐

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1		!
		!
IND #	YES ☐	! NO ☐
		! Explain:

Investigation #2		!
		!
IND #	YES ☐	! NO ☐
		! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1
YES ☐
Explain:

!
!
! NO ☐
! Explain:

Investigation #2
YES ☐
Explain:

!
!
! NO ☐
! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES ☐ NO ☐

If yes, explain:

=====

Name of person completing form: Jagjit Grewal, MPH
Title: Senior Regulatory Health Project Manager
Date: November 1, 2012

Name of Office/Division Director signing form: Donna Griebel, MD
Title: Director, Division of Gastroenterology and Inborn Errors Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JAGJIT S GREWAL
11/02/2012

DONNA J GRIEBEL
11/02/2012

EXCLUSIVITY SUMMARY

NDA # 203050

SUPPL #

HFD # 180

Trade Name

Generic Name Palonosetron Hydrochloride Injection

Applicant Name Dr. Reddy's Laboratories Limited

Approval Date, If Known March 1, 2016

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒ NO ☐

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(2)

b) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES ☐ NO ☒

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

Not applicable (N/A)

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

N/A

c) Did the applicant request exclusivity?

YES ☐ NO ☒

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

d) Has pediatric exclusivity been granted for this Active Moiety?

YES ☒ NO ☐

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

NO

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES ☐ NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

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1. Single active ingredient product.

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YES ☒ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#	021372	Aloxi (palonosetron hydrochloride) injection
NDA#	022233	Aloxi (palonosetron hydrochloride) capsule
NDA#	205718	Akynzeo (netupitant and palonosetron) capsule

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES ☐ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

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is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

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IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES ☐ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES ☐ NO ☐

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES ☐ NO ☐

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES ☐ NO ☐

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1		!
		!
IND #	YES ☐	! NO ☐
		! Explain:

Investigation #2		!
		!
IND #	YES ☐	! NO ☐
		! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1
YES ☐
Explain:

!
!
! NO ☐
! Explain:

Investigation #2
YES ☐
Explain:

!
!
! NO ☐
! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES ☐ NO ☐

If yes, explain:

=====

Name of person completing form: Mary Chung, PharmD.
Title: Regulatory Project Manager
Date: 2/29/16

Name of Office/Division Director signing form: Donna Griebel, M.D.
Title: Director, Division of Gastroenterology and Inborn Errors Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARY H CHUNG
03/01/2016

DONNA J GRIEBEL
03/01/2016

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 203050 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: Not applicable Established/Proper Name: Palonosetron Hydrochloride Dosage Form: injection		Applicant: Dr. Reddy's Laboratories Limited Agent for Applicant (if applicable): Dr. Reddy's Laboratories, Inc.
RPM: Mary Chung		Division: Division of Gastroenterology and Inborn Errors Products
NDA Application Type: ☐ 505(b)(1) ☒ 505(b)(2) Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2) BLA Application Type: ☐ 351(k) ☐ 351(a) Efficacy Supplement: ☐ 351(k) ☐ 351(a)		<u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u> - Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. - Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) ☒ No changes ☐ New patent/exclusivity <i>(notify CDER OND IO)</i> Date of check: March 1, 2016 <i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i>
❖ Actions		
- Proposed action - User Fee Goal Date is <u>March 1, 2016</u>		☒ AP ☐ TA ☐ CR
Previous actions <i>(specify type and date for each action taken)</i>		☐ None 11/2/12, TA
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		☐ Received
❖ Application Characteristics ³		

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

² For resubmissions, 505(b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA.

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only): Type 5
(confirm chemical classification at time of approval)

- | | |
|---|---|
| ☐ Fast Track | ☐ Rx-to-OTC full switch |
| ☐ Rolling Review | ☐ Rx-to-OTC partial switch |
| ☐ Orphan drug designation | ☐ Direct-to-OTC |
| ☐ Breakthrough Therapy designation | |

(NOTE: Set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager;
Refer to the "RPM BT Checklist for Considerations after Designation Granted" for other required actions: [CST SharePoint](#))

NDAs: Subpart H

- ☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)

Subpart I

- ☐ Approval based on animal studies

- ☐ Submitted in response to a PMR
☐ Submitted in response to a PMC
☐ Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- ☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)

Subpart H

- ☐ Approval based on animal studies

- REMS: ☐ MedGuide
☐ Communication Plan
☐ ETASU
☐ MedGuide w/o REMS
☐ REMS not required

Comments:

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (approvals only)	☐ Yes ☐ No
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	☒ Yes ☐ No
• Indicate what types (if any) of information were issued	☒ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)? • If so, specify the type	☒ No ☐ Yes
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
CONTENTS OF ACTION PACKAGE	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (approvals only)	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included

Action Letters	
❖ Copies of all action letters (including approval letter with final labeling)	Approval 3/1/2016 Tentative approval 11/2/2012
Labeling	
❖ Package Insert (write submission/communication date at upper right of first page of PI)	
• Most recent draft labeling (if it is division-proposed labeling, it should be in track-changes format)	☒ Included
• Original applicant-proposed labeling	☒ Included
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (write submission/communication date at upper right of first page of each piece)	☐ Medication Guide ☒ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☐ None
• Most-recent draft labeling (if it is division-proposed labeling, it should be in track-changes format)	☒ Included
• Original applicant-proposed labeling	☒ Included
❖ Labels (full color carton and immediate-container labels) (write submission/communication date on upper right of first page of each submission)	
• Most-recent draft labeling	☒ Included
❖ Proprietary Name	Applicant did not request proprietary name.
• Acceptability/non-acceptability letter(s) (indicate date(s))	
• Review(s) (indicate date(s))	
❖ Labeling reviews (indicate dates of reviews)	RPM: ☒ None DMEPA: ☐ None 1/19/16 DMPP/PLT (DRISK): ☐ None 2/10/16 OPDP: ☐ None 2/2/16 SEALD: ☒ None CSS: ☒ None Product Quality ☒ None Other: ☐ None Pediatric: 2/18/16; Maternal Health: 1/25/16; ClinPharm: 2/9/16
Administrative / Regulatory Documents	
❖ RPM Filing Review ⁴ /Memo of Filing Meeting (indicate date of each review)	505(b)(2) Clearance Committee: 3/1/16
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	☐ Not a (b)(2)
❖ NDAs only: Exclusivity Summary (signed by Division Director)	☒ Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	

⁴ Filing reviews for scientific disciplines are NOT required to be included in the action package.

Applicant is on the AIP	☐ Yes ☒ No
- This application is on the AIP - If yes, Center Director's Exception for Review memo (indicate date) - If yes, OC clearance for approval (indicate date of clearance communication)	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics (approvals only) Date reviewed by PeRC _____ If PeRC review not necessary, explain: <i>This application does not include a new active ingredient, a new indication, a new dosage form, a new dosing regimen or a new route of administration. Therefore, the application does not trigger PREA.</i>	
❖ Breakthrough Therapy Designation	☒ N/A
Breakthrough Therapy Designation Letter(s) (granted, denied, an/or rescinded)	
CDER Medical Policy Council Breakthrough Therapy Designation Determination Review Template(s) (include only the completed template(s) and not the meeting minutes)	
CDER Medical Policy Council Brief – Evaluating a Breakthrough Therapy Designation for Rescission Template(s) (include only the completed template(s) and not the meeting minutes) <i>(completed CDER MPC templates can be found in DARRTS as clinical reviews or on the MPC SharePoint Site)</i>	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, Formal Dispute Resolution Request decisional letters, etc.) (do not include OPDP letters regarding pre-launch promotional materials as these are non-disclosable; do not include Master File letters; do not include previous action letters, as these are located elsewhere in package)	2/29/16, 2/25/16, 2/24/16, 2/22/16, 2/18/16, 2/11/16, 1/25/16, 1/20/16, 10/15/15
❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)	
❖ Minutes of Meetings	
If not the first review cycle, any end-of-review meeting (indicate date of mtg)	☒ N/A or no mtg
Pre-NDA/BLA meeting (indicate date of mtg)	☒ No mtg
EOP2 meeting (indicate date of mtg)	☒ No mtg
Mid-cycle Communication (indicate date of mtg)	☒ N/A
Late-cycle Meeting (indicate date of mtg)	☒ N/A
Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings) (indicate dates of mtgs)	

❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	☒ None
Division Director Summary Review (<i>indicate date for each review</i>)	☐ None 3/1/2016
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	☐ None 3/1/2016
PMR/PMC Development Templates (<i>indicate total number</i>)	☒ None
Clinical	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	☒ No separate review
• Clinical review(s) (<i>indicate date for each review</i>)	2/29/16
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	☐ None Not applicable
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☐ and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	Not applicable
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>) ⁵	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	☒ N/A
❖ Risk Management - REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>) - REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) - Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)	☒ None
❖ OSI Clinical Inspection Review Summary(ies) (<i>include copies of OSI letters to investigators</i>)	☒ None requested
Clinical Microbiology ☒ None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	☐ No separate review
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	☐ None
Biostatistics ☒ None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	☐ No separate review
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	☐ No separate review
Statistical Review(s) (<i>indicate date for each review</i>)	☐ None

⁵ For Part 3 combination products, all reviews from the reviewing Center(s) should be entered into the official archive (for further instructions, see "Section 508 Compliant Documents: Process for Regulatory Project Managers" located in the CST electronic repository).

Clinical Pharmacology		☒ None
❖ Clinical Pharmacology Division Director Review(s) <i>(indicate date for each review)</i>		☐ No separate review
Clinical Pharmacology Team Leader Review(s) <i>(indicate date for each review)</i>		☐ No separate review
Clinical Pharmacology review(s) <i>(indicate date for each review)</i>		☐ None
❖ OSI Clinical Pharmacology Inspection Review Summary <i>(include copies of OSI letters)</i>		☐ None requested
Nonclinical		☒ None
❖ Pharmacology/Toxicology Discipline Reviews		
• ADP/T Review(s) <i>(indicate date for each review)</i>		☐ No separate review
• Supervisory Review(s) <i>(indicate date for each review)</i>		☐ No separate review
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>		☐ None
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer <i>(indicate date for each review)</i>		☐ None
❖ Statistical review(s) of carcinogenicity studies <i>(indicate date for each review)</i>		☐ No carc
❖ ECAC/CAC report/memo of meeting		☐ None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary <i>(include copies of OSI letters)</i>		☐ None requested
Product Quality		☐ None
❖ Product Quality Discipline Reviews ⁶		
• Tertiary review <i>(indicate date for each review)</i>		☒ None
• Secondary review (e.g., Branch Chief) <i>(indicate date for each review)</i>		☒ None
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) <i>(indicate date for each review)</i>		☐ None 3/1/16, 2/24/16, 2/9/16
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team <i>(indicate date of each review)</i>		☒ None
❖ Environmental Assessment (check one) (original and supplemental applications)		
☒ Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>		8/10/2012
☐ Review & FONSI <i>(indicate date of review)</i>		
☐ Review & Environmental Impact Statement <i>(indicate date of each review)</i>		
❖ Facilities Review/Inspection		
☒ Facilities inspections <i>(action must be taken prior to the re-evaluation date) (only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change))</i>		☒ Acceptable Re-evaluation date: ☐ Withhold recommendation ☐ Not applicable

⁶ Do not include Master File (MF) reviews or communications to MF holders. However, these documents should be made available upon signatory request.

Day of Approval Activities	
❖ For all 505(b)(2) applications: Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)	☒ No changes ☐ New patent/exclusivity (<i>Notify CDER OND IO</i>)
Finalize 505(b)(2) assessment	☒ Done
❖ For Breakthrough Therapy (BT) Designated drugs: Notify the CDER BT Program Manager	☐ Done (<i>Send email to CDER OND IO</i>)
❖ For products that need to be added to the flush list (generally opioids): Flush List Notify the Division of Online Communications, Office of Communications	☐ Done
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	☒ Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	☐ Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	☐ Done
❖ Ensure Pediatric Record is accurate	☐ Done
❖ Send approval email within one business day to CDER-APPROVALS	☒ Done

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/s/

MARY H CHUNG
03/07/2016

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: March 1, 2016

FROM: Division of Gastroenterology and Inborn Errors Products (DGIEP)

TO: NDA 203050 Dr. Reddy's Labs' (Dr. Reddy's)
Palonosetron Hydrochloride Injection, 0.05 mg/mL, 1.5 mL and 5 mL vials

RE: Pending Citizen Petition for Aloxi (palonosetron hydrochloride) Injection
(FDA-2016-P-0621)

This memorandum documents DGIEP's awareness of a pending citizen petition regarding Eloxi's pending 505(b)(2) application (NDA 207963) that relies on Aloxi (palonosetron hydrochloride) Injection as a listed drug; and CDER's determination that the issues raised in the petition are not implicated by FDA's approval of Dr. Reddy's 505(b)(2) NDA 203050 that relies on Aloxi.

Background

A citizen petition (Docket No. FDA-2016-P-0621) dated February 18, 2016, was submitted by Hogan Lovells US LLP on behalf of Helsinn Healthcare SA (Helsinn) requesting that the Food and Drug Administration (FDA) take certain actions with respect to a 505(b)(2) application submitted by Exela Pharma Sciences, LLC (Exela) (NDA 207963), which relies on Aloxi as a listed drug to support approval of the proposed palonosetron product. Specifically, Helsinn asks that:

1. [T]he Commissioner of [FDA] not approve Exela's NDA 207963 because the proposed product's high concentration of active ingredient compared to the reference product, Aloxi, creates an unacceptable and unnecessary risk of medication error, particularly with respect to pediatric patients.
2. Alternatively, if FDA determines that, notwithstanding the risk of medication error, Exela's proposed product may be considered for approval, that the Commissioner:

- a. require Exela to support its proposed formulation with human bioequivalence data;
- b. require Exela to demonstrate the safety of its proposed formulation with adequate testing, including human testing in the relevant patient population; and
- c. not rate Exela's proposed product as therapeutically equivalent to Aloxi due to the difference in concentration between the products.

The petition (pp. 7-9) states that Exela's product has a concentration that is 2.5 times greater than Aloxi; and alleges that the difference in concentration creates a risk of medication error related to the dosing of pediatric patients because the pediatric indication is protected by Helsinn's exclusivity and will likely be carved out of the labeling. The petition (pp. 5, 12-17) also expresses concern regarding significant differences between the excipients in the formulations, differences in osmolality between the two products, and questions whether there are differences in pH range between the products. The petition (pp. 14-15) also states that because of these differences between the products, Exela should provide human bioequivalence data to support reliance on Aloxi as the listed drug in support of approval or conduct independent clinical studies showing that the product is safe and effective.

Discussion

Although the requested actions set forth in the Helsinn petition expressly relate only to the Exela application, the Agency has nonetheless considered the issues raised in the petition as they relate to Dr. Reddy's NDA 203050 for Palonosetron Hydrochloride Injection, 0.05 mg/mL, 1.5 mL and 5 mL vials, which is also a 505(b)(2) application that relies on Aloxi as a listed drug. Upon review of the petition and Dr. Reddy's NDA 203050, DGIEP in consultation with the Office of Regulatory Policy and other components, has determined that issues raised in the petition do not necessitate delay in approval of Dr. Reddy's product as summarized below.

Dr. Reddy's product contains the same drug concentration as Aloxi, is isotonic like Aloxi, and has the same pH range as Aloxi (4.5 – 5.5). Dr. Reddy's has also submitted adequate stability data for its NDA. While Dr. Reddy's formulation is similar to Aloxi in a number of ways (b) (4) it contains sodium acetate instead of the sodium citrate (b) (4) in Aloxi) and does not contain EDTA. We have concluded that this difference in formulation is not expected to impact pharmacologic characteristics of the product and the relative bioavailability is expected to be comparable. Thus there is sufficient information to bridge to the Agency's previous finding of safety and effectiveness for the listed drug Aloxi to support approval of Dr. Reddy's application. An in vivo pharmacokinetic study is not needed to establish a scientific bridge to Aloxi.

Given that Dr. Reddy's product has the same drug concentration as Aloxi, the petitioner's assertions regarding the potential risk of medication errors due to differences in concentration are not implicated here.

Thus, the primary issues raised in the citizen petition and the actions requested are not implicated by the Agency's approval of Dr. Reddy's NDA. It is not appropriate to delay approval of the application to prepare a response to the citizen petition.

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/s/

MARY H CHUNG
03/01/2016

DANUTA E GROMEK-WOODS
03/01/2016

DONNA J GRIEBEL
03/01/2016

From: [Chung, Mary](#)
To: [Java Lakshmi \(javalakshmia@drreddys.com\)](#)
Cc: [Srinivasa Rao \(srao@drreddys.com\)](#); [Chung, Mary](#)
Subject: NDA 203050 palonosetron - FDA proposed PPI
Date: Monday, February 29, 2016 6:13:33 PM
Attachments: [NDA 203050 palonosetron FDA proposed PPI 2-29-16 tracked changes.doc](#)
[NDA 203050 palonosetron FDA proposed PPI 2-29-16 tracked changes.pdf](#)
[NDA 203050 palonosetron FDA proposed PPI 2-29-16 clean.doc](#)
[NDA 203050 palonosetron FDA proposed PPI 2-29-16 clean.pdf](#)

Good afternoon,

Reference is made to your September 1, 2015 resubmission to your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for palonosetron hydrochloride injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL.

On February 26, 2016, we received your proposed labeling submission to this application, and have proposed revisions that are included as an enclosure (PPI). We request that you resubmit labeling (PPI) that addresses these issues by March 1, 2016.

Please confirm receipt of this correspondence.

Regards,
Mary

Mary Chung, PharmD.
Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III, CDER/ FDA

10903 New Hampshire Avenue, Bldg. 22, Room 5350
Phone: 301-796-0260 /fax: 301-796-9904
mary.chung@fda.hhs.gov

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4 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

MARY H CHUNG
02/29/2016

From: [Chung, Mary](#)
To: [Java Lakshmi \(javalakshmia@drreddys.com\)](#)
Cc: [Srinivasa Rao \(srao@drreddys.com\)](#); [Chung, Mary](#)
Subject: NDA 203050 palonosetron - FDA Proposed PI and PPI
Date: Thursday, February 25, 2016 5:58:44 PM
Attachments: [NDA 203050 palonosetron FDA proposed PI 2-25-15 tracked changes.docx](#)
[NDA 203050 palonosetron FDA proposed PI 2-25-15 tracked changes.pdf](#)
[NDA 203050 palonosetron FDA proposed PI 2-25-15 clean copy.docx](#)
[NDA 203050 palonosetron FDA proposed PI 2-25-15 clean copy.pdf](#)
[NDA 203050 palonosetron FDA proposed PPI 2-25-16.doc](#)
[NDA 203050 palonosetron FDA proposed PPI 2-25-16.pdf](#)

Good afternoon,

Reference is made to your September 1, 2015 resubmission to your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for palonosetron hydrochloride injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL.

On February 16, 2016, we received your proposed labeling submission to this application, and have proposed revisions that are included as an enclosure (PI). We request that you resubmit labeling (PI, PPI) that addresses these issues by Friday February 26, 2016.

Your proposed prescribing information (PI) must conform to the content and format regulations found at [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). Prior to resubmitting your proposed PI, we encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances.
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

At the end of labeling discussions, use the SRPI checklist to ensure that the PI conforms with format items in regulations and guidances.

Please confirm receipt of this correspondence.

Regards,
Mary

Mary Chung, PharmD.
Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III, CDER/ FDA

10903 New Hampshire Avenue, Bldg. 22, Room 5350
Phone: 301-796-0260 /fax: 301-796-9904
mary.chung@fda.hhs.gov

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/s/

MARY H CHUNG
02/25/2016

From: [Chung, Mary](#)
To: [Java Lakshmi \(javalakshmia@drreddys.com\)](#)
Cc: [Srinivasa Rao \(srao@drreddys.com\)](#); [Chung, Mary](#)
Subject: NDA 203050 palonosetron I.V.- Information Request
Date: Wednesday, February 24, 2016 2:32:35 PM

Good afternoon,

Reference is made to your September 1, 2015 resubmission to your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for palonosetron hydrochloride injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL.

In your response received February 23, 2016 to our February 22, 2016 Information Request, you have stated the following: "During the review of the available literature, we did not identify any new/ significant safety information that would have an impact on the labeling or safety profile of Palonosetron."

Please clarify the criteria you used to define "significant safety information".

Please provide your response to the NDA by February 25, 2016, or before, as soon as able.

Please confirm receipt of this correspondence.

Regards,
Mary

Mary Chung, PharmD.
Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III, CDER/ FDA

10903 New Hampshire Avenue, Bldg. 22, Room 5350
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/s/

MARY H CHUNG
02/24/2016

From: [Chung, Mary](#)
To: [Java Lakshmi \(javalakshmia@drreddys.com\)](#)
Cc: [Srinivasa Rao \(srao@drreddys.com\)](#); [Chung, Mary](#)
Subject: NDA 203050 palonosetron I.V.- Information Request
Date: Monday, February 22, 2016 11:08:43 AM

Good morning,

Reference is made to your September 1, 2015 resubmission to your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for palonosetron hydrochloride injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL.

Additional reference is made to the November 2, 2012 tentative approval issued for this NDA. This November 2, 2012 tentative approval letter indicated "In addition to a safety update, the amendment ["request for final approval"] should also identify changes, if any, in the conditions under which your product was tentatively approved..."

You have not provided this safety update in your September 1, 2015 request for final approval. Please submit the safety update requested in the November 2, 2012 tentative approval letter to the NDA by 2/23/16.

Please also include in your 2/23/16 response to the above information request, a 4-month safety update report according 21 CFR 314.50(d)(5)(vi)(b).

Please confirm receipt of this message.

Regards,
Mary

Mary Chung, PharmD.
Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III, CDER/ FDA

10903 New Hampshire Avenue, Bldg. 22, Room 5350
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MARY H CHUNG
02/22/2016

From: [Chung, Mary](#)
To: [Java Lakshmi \(javalakshmia@drreddys.com\)](#)
Cc: [Srinivasa Rao \(srao@drreddys.com\)](#); [Chung, Mary](#)
Subject: NDA 203050 palonosetron - Label: Carton/Container
Date: Thursday, February 18, 2016 1:07:11 PM

Good afternoon,

Reference is made to your September 1, 2015 resubmission to your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for palonosetron hydrochloride injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL.

On January 29, 2015, we received your proposed carton/container labeling submission to this application, and have the below additional comment. We request that you resubmit carton/container labeling that addresses these issues by Monday February 22, 2016, or before.

We acknowledge your effort to add the net quantity statement to the PDP as (b) (4)
(b) (4) Please refer to 21 CFR 201.51 and revise the statement (b) (4) with the actual quantity of the vial. For example, the net quantity statement should state "5 mL single dose vial".

Please confirm receipt of this correspondence.

Regards,
Mary

Mary Chung, PharmD.
Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III, CDER/ FDA

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MARY H CHUNG
02/23/2016

From: [Chung, Mary](#)
To: [Java Lakshmi \(javalakshmia@drreddys.com\)](#); [Srinivasa Rao \(srao@drreddys.com\)](#)
Cc: [Chung, Mary](#)
Subject: NDA 203050 palonosetron - FDA proposed PI and PPI
Date: Thursday, February 11, 2016 4:48:47 PM
Attachments: [NDA 203050 palonosetron FDA Proposed PI 2-11-16 clean copy.docx](#)
[NDA 203050 palonosetron FDA Proposed PI 2-11-16 clean copy.pdf](#)
[NDA 203050 palonosetron FDA Proposed PI 2-11-16 tracked changes.docx](#)
[NDA 203050 palonosetron FDA Proposed PI 2-11-16 tracked changes.pdf](#)
[NDA 203050 palonosetron FDA proposed PPI 2-11-16 clean.doc](#)
[NDA 203050 palonosetron FDA proposed PPI 2-11-16 clean.pdf](#)
[NDA 203050 palonosetron FDA proposed PPI 2-11-16.doc](#)
[NDA 203050 palonosetron FDA proposed PPI 2-11-16.pdf](#)

Good afternoon,

Reference is made to your September 1, 2015 resubmission to your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for palonosetron hydrochloride injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL.

On November 4, 2015, we received your proposed labeling submission to this application, and have proposed revisions that are included as an enclosure (PI, PPI). We request that you resubmit labeling (PI, PPI) that addresses these issues by Tuesday February 16, 2016.

Your proposed prescribing information (PI) must conform to the content and format regulations found at [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). Prior to resubmitting your proposed PI, we encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances.
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

At the end of labeling discussions, use the SRPI checklist to ensure that the PI conforms with format items in regulations and guidances.

Regards,
Mary

Mary Chung, PharmD.
Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III, CDER/ FDA

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/s/

MARY H CHUNG
02/11/2016

From: [Chung, Mary](#)
To: [Java Lakshmi \(javalakshmia@drreddys.com\)](#)
Cc: [Srinivasa Rao \(srao@drreddys.com\)](#); [Chung, Mary](#)
Subject: NDA 203050 palonosetron I.V.- Carton/Container Label
Date: Monday, January 25, 2016 1:54:45 PM
Attachments: [1-25-16 NDA 203050 carton container label FDA Comments.pdf](#)

Good afternoon,

Reference is made to your September 1, 2015 resubmission to your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for palonosetron hydrochloride injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL.

On November 4, 2015, we received your proposed carton/container label submission to this application, and have the attached comments and recommendations.

We request that you resubmit carton/container labeling that addresses these issues by February 1, 2016.

Regards,
Mary

Mary Chung, PharmD.
Regulatory Health Project Manager
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Office of Drug Evaluation III, CDER/ FDA

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Comments/ Recommendations on Carton/Container Label for NDA 203050

1. Revise the font color of the established name (blue color) or revise the color scheme of the strengths ((b) (4) color). (b) (4)
(b) (4)
The use of the (b) (4) color font for the established name and the product strengths minimizes the difference between the strengths, which may lead to wrong strength selection errors.
2. There is inadequate differentiation between the 0.075 mg/1.5 mL and 0.25 mg/5 mL strengths. Consider (b) (4) increasing the font size or some other means to provide adequate differentiation between the vial and container labels.
3. For the vial labels, consider decreasing the prominence of the storage statement by decreasing the font size. Established name and strength should be the most prominent information on the vial and container labels.
4. As currently presented, the product code in the NDC number for 0.25 mg/5 mL strength (- (b) (4) the product code in the NDC number for 0.075 mg/1.5 mL strength (- (b) (4) -). This can lead to wrong strength errors because barcode scanners may only read (b) (4) the NDC codes (i.e. (b) (4)) and pharmacists may rely on the (b) (4) portion as a manual check. Therefore, we recommend that you revise the product code in the NDC numbers (b) (4)
5. Add a net quantity statement to the principal display panel (PDP) in accordance with 21 CFR 201.51. We recommend that the net quantity statement be located away from the product strength and with less prominence. For example, the statement can be added to the bottom right corner of the PDP across from the Rx only statement with same font size and type as the “Rx only” statement.
6. Delete the (b) (4) statement (b) (4).
7. Revise the (b) (4) statement to “Single dose vial(s)” since the term “single dose” accurately describes the correct usage of this product in a single patient as a single injection.¹
8. If space permits, consider adding the usual dosage statement on the side panel of the vial label. For example, “Usual dose: See prescribing information”.

References:

1. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM468228.pdf>

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/s/

MARY H CHUNG
01/26/2016

Chung, Mary

From: Chung, Mary
Sent: Wednesday, January 20, 2016 12:10 PM
To: Jaya Lakshmi (jayalakshmia@drreddys.com)
Cc: Srinivasa Rao (srao@drreddys.com); Chung, Mary
Subject: NDA 203050 palonosetron I.V.

Good afternoon,

Reference is made to your September 1, 2015 resubmission to your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for palonosetron hydrochloride injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL.

Additional reference is made to our October 15, 2015 correspondence, which requested documentation of notice re: patent 9066980, and patent certification and documentation of notice re: patent 9125905, be provided to the NDA. As previously indicated, your response to this request has not been received to the NDA.

On December 3, 2015, you indicated a patent amendment addressing the recently listed patents, patent 9125905 and 9173942, will be submitted. We request that you provide patent certification and documentation of notice for all timely listed unexpired patents. Please ensure your patent amendment addresses all outstanding required patent certification and documentation of notice for patent 9066980, 9125905, 9173942.

Regards,
Mary

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/s/

MARY H CHUNG
01/20/2016

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 203050 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type:
Proprietary Name: N/A Established/Proper Name: Palonosetron Hydrochloride Dosage Form: Injection		Applicant: Dr. Reddy's Laboratories Limited Agent for Applicant: Dr. Reddy's Laboratories, Inc.
RPM: Jagjit Grewal		Division: Division of Gastroenterology and Inborn Errors Products
<u>NDA and NDA Efficacy Supplements:</u> NDA Application Type: ☐ 505(b)(1) ☒ 505(b)(2) Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2) (A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.) <u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u> Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)): 021372 Aloxi (palonosetron hydrochloride) injection Provide a brief explanation of how this product is different from the listed drug. (b) (4) ☐ This application does not rely upon a listed drug. ☐ This application relies on literature. ☐ This application relies on a final OTC monograph. ☐ This application relies on (explain) <u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u> <u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u> ☒ No changes ☐ Updated Date of check: 11/2/12 If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.		

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 5) lists the documents to be included in the Action Package.

² For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

❖ Actions		
- Proposed action - User Fee Goal Date is <u>11/3/2012</u>	☐ AP ☒ TA ☐ CR	
Previous actions (<i>specify type and date for each action taken</i>)	☒ None	
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		☐ Received
❖ Application Characteristics ³		
Review priority: ☒ Standard ☐ Priority Chemical classification (new NDAs only): Type 5 ☐ Fast Track ☐ Rolling Review ☐ Orphan drug designation ☐ Rx-to-OTC full switch ☐ Rx-to-OTC partial switch ☐ Direct-to-OTC NDAs: Subpart H ☐ Accelerated approval (21 CFR 314.510) ☐ Restricted distribution (21 CFR 314.520) Subpart I ☐ Approval based on animal studies ☐ Submitted in response to a PMR ☐ Submitted in response to a PMC ☐ Submitted in response to a Pediatric Written Request BLAs: Subpart E ☐ Accelerated approval (21 CFR 601.41) ☐ Restricted distribution (21 CFR 601.42) Subpart H ☐ Approval based on animal studies REMS: ☐ MedGuide ☐ Communication Plan ☐ ETASU ☐ MedGuide w/o REMS ☒ REMS not required Comments:		
❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)		☐ Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)		☐ Yes ☐ No
❖ Public communications (<i>approvals only</i>)		
Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No	
Press Office notified of action (by OEP)	☐ Yes ☒ No	
Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ HHS Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other	

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

❖ Exclusivity	
Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i>	☒ No ☐ Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
(b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i>	☒ No ☐ Yes If yes, NDA # _____ and date exclusivity expires: _____
(b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i>	☒ No ☐ Yes If yes, NDA # _____ and date exclusivity expires: _____
(b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i>	☒ No ☐ Yes If yes, NDA # _____ and date exclusivity expires: _____
NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</i>	☒ No ☐ Yes If yes, NDA # _____ and date 10-year limitation expires: _____
❖ Patent Information (NDAs only)	
Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(i)(A) ☒ Verified 21 CFR 314.50(i)(1) ☐ (ii) ☐ (iii)
[505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	☐ No paragraph III certification Date patent will expire: 4/13/2015
[505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i>	☐ N/A (no paragraph IV certification) ☒ Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for **each** paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

☒ Yes ☐ No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "**Yes**," skip to question (4) below. If "**No**," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

☐ Yes ☐ No

If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "**No**," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

☐ Yes ☐ No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "**No**," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

☐ Yes ☒ No

If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "**No**," continue with question (5).

(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period). <i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i> <i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i>	☒ Yes ☐ No
CONTENTS OF ACTION PACKAGE	
❖ Copy of this Action Package Checklist⁴	11/6/2012
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	☐ Included (N/A as this is a tentative approval)
Documentation of consent/non-consent by officers/employees	☐ Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) Tentative Approval 11/2/2012
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	10/16/2012
Original applicant-proposed labeling	1/3/2012
Example of class labeling, if applicable	Aloxi injection 2/29/2008 Zofran injection 9/14/2011 Kytril injection 4/29/2011

⁴ Fill in blanks with dates of reviews, letters, etc.

❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>)	☐ Medication Guide ☒ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☐ None
• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	10/29/2012
• Original applicant-proposed labeling	1/3/2012
• Example of class labeling, if applicable	Aloxi injection 2/29/2008
❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)	
• Most-recent draft labeling	10/16/2012
❖ Proprietary Name • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) • Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name.	N/A – no proprietary name has been proposed
❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)	☒ RPM 3/14/2012 ☒ DMEPA 10/1/2012 ☒ DMPP/PLT 8/10/2012 ☒ ODPD (DDMAC) 8/3/2012 ☐ SEALD ☐ CSS ☐ Other reviews
Administrative / Regulatory Documents	
❖ Administrative Reviews (<i>e.g., RPM Filing Review⁵/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)	3/14/2012
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte	☐ Not a (b)(2) 9/24/2012
❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)	☐ Not a (b)(2) 11/1/2012
❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)	☒ Included 11/2/2012
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics (<i>approvals only</i>) • Date reviewed by PeRC _____ If PeRC review not necessary, explain: <u>The application did not propose a new active ingredient, dosage form, route of administration, indication, or dosing regimen in comparison to the listed drug.</u> • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>)	☐ Included (N/A)

⁵ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent <i>(include certification)</i>	☒ Verified, statement is acceptable
❖ Outgoing communications <i>(letters, including response to FDRR (do not include previous action letters in this tab), emails, faxes, telecons)</i>	10/25/2012 PPI comments 10/10/2012 PI-Cart-Cont comment 10/2/2012 Cart-Cont comments 9/20/2012 PI Label comments 5/23/2012 CMC IR 3/14/2012 Filing communication 1/13/2012 Acknowledgement
❖ Internal memoranda, telecons, etc.	N/A
❖ Minutes of Meetings	
• Regulatory Briefing <i>(indicate date of mtg)</i>	☒ No mtg
• If not the first review cycle, any end-of-review meeting <i>(indicate date of mtg)</i>	☒ N/A or no mtg
• Pre-NDA/BLA meeting <i>(indicate date of mtg)</i>	☒ No mtg
• EOP2 meeting <i>(indicate date of mtg)</i>	☒ No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) <i>(indicate dates of mtgs)</i>	none
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available <i>(do not include transcript)</i>	
Decisional and Summary Memos	
❖ Office Director Decisional Memo <i>(indicate date for each review)</i>	☒ None
Division Director Summary Review <i>(indicate date for each review)</i>	☐ None 11/2/2012
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	☐ None 10/31/2012
PMR/PMC Development Templates <i>(indicate total number)</i>	☒ None
Clinical Information⁶	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) <i>(indicate date for each review)</i>	Co-signed primary reviews
• Clinical review(s) <i>(indicate date for each review)</i>	10/22/2012, 3/2/2012
• Social scientist review(s) (if OTC drug) <i>(indicate date for each review)</i>	☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☒ and include a review/memo explaining why not <i>(indicate date of review/memo)</i>	See 10/22/2012 review page 15
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers <i>(indicate date of each review)</i>	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation <i>(indicate date of each review)</i>	☒ Not applicable

⁶ Filing reviews should be filed with the discipline reviews.

❖ Risk Management - REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>) - REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) - Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)	N/A N/A ☒ None
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	☒ None requested
Clinical Microbiology ☒ None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	☐ None
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	☐ None
Biostatistics ☒ None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	☐ None
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	☐ None
Statistical Review(s) (<i>indicate date for each review</i>)	☐ None
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	☒ None
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	☐ None Co-signed primary reviews
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	☐ None 10/2/2012, 3/7/2012
❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)	☒ None
Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	☒ None
• Supervisory Review(s) (<i>indicate date for each review</i>)	☐ None Co-signed primary reviews
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	☐ None 9/13/2012, 2/15/2012
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	☒ None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)	☒ None requested

Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>	☒ None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>	☐ None Co-signed primary reviews
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>	☐ None 10/22/2012, 8/10/2012, 6/21/2012, 3/21/2012, 3/2/2012
❖ Microbiology Reviews ☐ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i> ☐ BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>	☐ Not needed 3/20/2012, 2/16/2012
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>	☒ None
❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>	See 8/10/2012 review, page 45
☐ Review & FONSI <i>(indicate date of review)</i>	
☐ Review & Environmental Impact Statement <i>(indicate date of each review)</i>	
❖ Facilities Review/Inspection	
☒ NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁷)</i>	Date completed: 2/24/2012 ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER <i>(date of most recent TB-EER must be within 30 days of action date) (original and supplemental BLAs)</i>	Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation <i>(check box only, do not include documents)</i>	☐ Completed ☐ Requested ☐ Not yet requested ☒ Not needed (per review)

⁷ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication **AND** a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

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/s/

JAGJIT S GREWAL
11/06/2012

Grewal, Jagjit

From: Grewal, Jagjit
Sent: Thursday, October 25, 2012 10:51 AM
To: lsubramanian@drreddys.com
Cc: lbanks@drreddys.com; Grewal, Jagjit
Subject: NDA 203050 Palonosetron HCl - FDA PPI label revisions

Importance: High

Attachments: N203050 Palonosetron HCl - FDA PPI revisions 10.25.12.doc

Dear Ms. Subramanian,

Reference is made to your new drug application dated January 3, 2012, for NDA 203050 Palonosetron Hydrochloride injection. Attached is an annotated WORD document containing the FDA's revisions to your proposed patient package insert label.

Please review the indicated revisions and respond with your acceptance and/or proposed changes by Monday, October 29, 2012. Additionally, please acknowledge receipt of this correspondence.

I can be reached via email at the below phone number with any questions.



N203050
lonosetron HCl - FD/

Regards,

Jagjit Grewal, M.P.H.
Senior Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
CDER/OND/ODE III
Food & Drug Administration

Phone: (301) 796-0846 || Fax: (301) 796-9904
Email: Jagjit.Grewal@fda.hhs.gov

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/s/

JAGJIT S GREWAL
10/25/2012

Chung, Mary

From: Chung, Mary
Sent: Thursday, October 15, 2015 9:33 AM
To: Jaya Lakshmi (jayalakshmia@drreddys.com)
Cc: Srinivasa Rao; Chung, Mary
Subject: NDA 203050 palonosetron I.V.

Dear Jaya,
Reference is made to NDA 203050 palonosetron I.V.

Please provide to the NDA, documentation of notice re: patent 9066980, and patent certification and documentation of notice re: patent 9125905.

Regards,
Mary

Mary Chung, PharmD.
Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III, CDER/ FDA

10903 New Hampshire Avenue, Bldg. 22, Room 5350
Phone: 301-796-0260 /fax: 301-796-9904
mary.chung@fda.hhs.gov

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/s/

MARY H CHUNG
01/20/2016

Grewal, Jagjit

From: Grewal, Jagjit
Sent: Wednesday, October 10, 2012 2:07 PM
To: lbanks@drreddys.com
Cc: ctiruvattar@drreddys.com; Grewal, Jagjit
Subject: NDA 203050 Palonosetron HCl Injection - FDA PI & carton/container label revisions

Importance: High

Attachments: FDA PI Label Revisions 10.10.12.doc

Dear Mr. Banks,

Reference is made to you January 3, 2012 New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Palonosetron Hydrochloride Injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL. We also refer to your submissions dated September 25, 2012 and October 5, 2012 containing your revised package insert label and carton and container labeling in response to FDA's label edits.

Attached are additional FDA edits regarding your proposed package insert label.



FDA PI Label
Revisions 10.10.1...

We also have the following comments and recommendations on your proposed carton and container labeling:

1. The graphic/logo at the top of both container labels should be minimized so that it is not more prominent than the established name.
2. The salt "Hydrochloride" should be spelled out on the carton labeling. Therefore, it will appear as "HCL" on the container label and "Hydrochloride" on the carton labeling.
3. For the 1.5 mL carton labeling only, separate the net quantity ("five") from the container type (b) (4). We recommend that the statement (b) (4) appear below the route of administration ("For Intravenous Use Only") and that the statement (b) (4) appear in the upper right hand corner just above the established name ("Palonosetron HCL Injection").

Please review these changes and respond with your acceptance and/or proposed revisions by Monday, October 8, 2012. Additionally, please acknowledge receipt of this correspondence.

I can be reached via email or at the below phone number with any questions.

Regards,

Jagjit Grewal, M.P.H.
Senior Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
CDER/OND/ODE III
Food & Drug Administration

Phone: (301) 796-0846 || Fax: (301) 796-9904
Email: Jagjit.Grewal@fda.hhs.gov

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/s/

JAGJIT S GREWAL
10/10/2012

Grewal, Jagjit

From: Grewal, Jagjit
Sent: Monday, October 01, 2012 3:40 PM
To: lbanks@drreddys.com
Cc: Grewal, Jagjit
Subject: NDA 203050 Palonosetron HCl Injection - FDA carton/container label revisions

Importance: High

Dear Mr. Banks,

Reference is made to you January 3, 2012 New Drug Application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Palonosetron Hydrochloride Injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL. We have the following comments and recommendations on your proposed carton and container labeling:

General Comments (All Container Labels and Carton Labeling):

1. Remove (b) (4)
2. The established name "Palonosetron Hydrochloride" should be presented on a single line.

Container Label (1.5 mL and 5 mL Single Dose Vials):

3. Revise and relocate the statement "For Intravenous Injection Only" to read "For Intravenous Use" and to appear below the concentration ('0.05 mg/mL') to improve its visibility and readability.
4. Revise the statement (b) (4) and relocate this statement to appear after the statement, (b) (4) is an assumed characteristic of an injectable product and the volume, ('1.5 mL' and '5 mL') is included in the total drug content and therefore they are unnecessary statements.
5. Add the statement (b) (4) to reinforce proper handling of this product.
6. Delete the statement (b) (4) from the side panel for the 1.5 mL vial size (see recommendation above).
7. To make room for important information on the principal display panel and to minimize clutter, revise the salt 'Hydrochloride' to read 'HCL'.
8. To make room for important information on the principal display pane (b) (4)

The following is an example of how the information may appear on the principal display panel (based upon recommendations 3 to 5 and 7):

Palonosetron HCL Injection
0.25 mg/5 mL
(0.05 mg/mL)
For Intravenous Use Only
(b) (4)

Carton Labeling (five 1.5 mL vials and 5 mL Single Dose Vials):

9. Revise the statement (b) (4) is an assumed characteristic of an injectable product and the volume, ('1.5 mL') is already included in the total drug content and therefore both of these statements are unnecessary.
10. Revise the statement (b) (4) is an assumed characteristic of an injectable product and the volume, ('5 mL') is already included in the total drug content and therefore both of these statements are unnecessary.
11. Revise the statement "For Intravenous Injection Only" to read "For Intravenous Use".

Please review the above comments and respond with your acceptance and/or proposed changes by Monday, October 8, 2012. Additionally, please acknowledge receipt of this correspondence.

I can be reached via email or at the below phone number with any questions.

Regards,

Jagjit Grewal, M.P.H.
Senior Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
CDER/OND/ODE III
Food & Drug Administration
Phone: (301) 796-0846 || Fax: (301) 796-9904
Email: Jagjit.Grewal@fda.hhs.gov

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/s/

JAGJIT S GREWAL
10/02/2012

Grewal, Jagjit

From: Grewal, Jagjit
Sent: Thursday, September 20, 2012 3:20 PM
To: kernst@drreddys.com
Cc: Grewal, Jagjit
Subject: NDA 203050 Palonosetron HCl - FDA PI label revisions

Importance: High

Attachments: FDA PI Label Revisions 9.20.12.doc

Hello Kim,

Reference is made to your new drug application dated January 3, 2012, for NDA 203050 Palonosetron Hydrochloride injection. Attached is an annotated WORD document containing the FDA's revisions to your proposed package insert label.

Please review the indicated revisions and respond with your acceptance and/or proposed changes by Thursday, September 27, 2012. Additionally, please acknowledge receipt of this correspondence.

I can be reached at the below phone number or through email with any questions.



FDA PI Label
Revisions 9.20.12...

Regards,

Jagjit Grewal, M.P.H.
Senior Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
CDER/OND/ODE III
Food & Drug Administration

Phone: (301) 796-0846 || Fax: (301) 796-9904
Email: Jagjit.Grewal@fda.hhs.gov

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/s/

JAGJIT S GREWAL
09/20/2012



NDA 203-050

INFORMATION REQUEST

Dr. Reddy's Laboratories Limited
Attention: Kimberly Ernst
Associate Director, Global Regulatory Affairs
200 Somerset Corporate Blvd. 7th Floor
Bridgewater, NJ 08807

Dear. Ms. Ernst:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Palonosetron Hydrochloride Injection , 0.075 mg/1.5 mL and 0.25 mg/ 5 mL.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

During the review of your application, it was noted that the stability batch RJ003 showed (b) (4) % of an unidentified impurity after 6 months at the accelerated conditions (b) (4). Exceeding the limit of 0.5% is considered to be a "significant change" as described in ICH Q1R(R2). Also noted was a similar amount of the unidentified impurity after 12 months at the long term conditions in the same batch. Please explain the observations and, if available, submit additional long term stability data of the same batch.

If you have any questions, call Cathy Tran-Zwanetz, Regulatory Project Manager, at (301) 796-3877.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Branch Chief, Branch IV
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

MOO JHONG RHEE

05/23/2012

Chief, Branch IV



NDA 203050

FILING COMMUNICATION

Dr. Reddy's Laboratories Limited
C/O Dr. Reddy's Laboratories, Inc.
Attention: Kimberly Ernst
Associate Director, Global Regulatory Affairs
200 Somerset Corporate Blvd, 7th Floor
Bridgewater, NJ 08807

Dear Ms. Ernst:

Please refer to your New Drug Application (NDA) dated January 3, 2012, received January 3, 2012, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Palonosetron Hydrochloride Injection, 0.075 mg/1.5 mL and 0.25 mg/5 mL.

We also refer to your amendments dated February 14, 2012 and February 21, 2012.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is November 3, 2012.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by October 5, 2012.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

During our preliminary review of your submitted labeling, we have identified the following labeling format issues:

1. The Highlights Limitation Statement is included twice at the beginning of the package insert label. The repeated statement should be removed.
2. The proposed label includes the “Recent Major Changes” section in the Highlights of Prescribing Information. This section only applies to NDA supplements, and should therefore be removed.
3. In the Highlights of Prescribing Information, the statement regarding reporting of “Suspected Adverse Reactions” is included twice. The repeated statement should be removed.
4. The header “17.2 FDA-APPROVED PATIENT LABELING” should be removed from the Table of Contents.
5. The header “PACKAGE LABEL.PRINCIPAL DISPLAY PANEL SECTION” should be removed from the Table of Contents.
6. The reference statement regarding FDA-approved patient labeling should be revised to read “See FDA-approved patient labeling (Patient Information)”.
7. Patient Information should not be a subsection under the Patient Counseling Information section. Rather, it should be included at the end of section 17 without numbering as a subsection.

We request that you resubmit labeling that addresses these issues by April 6, 2012. The resubmitted labeling will be used for further labeling discussions.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI), and patient PI. Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI) and patient PI, and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

If you have any questions, call Jagjit Grewal, Regulatory Project Manager, at (301) 796-0846.

Sincerely,

{See appended electronic signature page}

Donna Griebel, M.D.
Director
Division of Gastroenterology and Inborn
Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

BRIAN K STRONGIN
03/14/2012
Signing for Dr. Griebel



NDA 203050

NDA ACKNOWLEDGMENT

Dr. Reddy's Laboratories Limited
Attention: Kimberly Ernst
Associate Director, Global Regulatory Affairs
200 Somerset Corporate Blvd, 7th Floor
Bridgewater, NJ 08807

Dear Ms. Ernst:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Palonosetron Hydrochloride Injection, 0.075 mg/1.5 mL and
0.25 mg/5 mL

Date of Application: January 3, 2012

Date of Receipt: January 3, 2012

Our Reference Number: NDA 203050

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on March 3, 2012, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

Title VIII of FDAAA amended the PHS Act by adding new section 402(j) [42 USC § 282(j)], which expanded the current database known as ClinicalTrials.gov to include mandatory

registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices.

In addition to the registration and reporting requirements described above, FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, the certification must include the appropriate National Clinical Trial (NCT) numbers [42 USC § 282(j)(5)(B)].

You did not include such certification when you submitted this application. You may use Form FDA 3674, "Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank," [42 U.S.C. § 282(j)] to comply with the certification requirement. The form may be found at <http://www.fda.gov/opacom/morechoices/fdaforms/default.html>.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of FDAAA apply to any clinical trial(s) referenced in this application. Please note that FDA published a guidance in January 2009, "Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of the Food and Drug Administration Amendments Act of 2007," that describes the Agency's current thinking regarding the types of applications and submissions that sponsors, industry, researchers, and investigators submit to the Agency and accompanying certifications. Additional information regarding the certification form is available at:

<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCA/ct/SignificantAmendmentstotheFDCA/FoodandDrugAdministrationAmendmentsActof2007/ucm095442.htm>. Additional information regarding Title VIII of FDAAA is available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html>. Additional information for registering your clinical trials is available at the Protocol Registration System website <http://prsinfo.clinicaltrials.gov/>.

When submitting the certification for this application, **do not** include the certification with other submissions to the application. Submit the certification within 30 days of the date of this letter. In the cover letter of the certification submission clearly identify that it pertains to **NDA 203050** submitted on January 3, 2012, and that it contains the FDA Form 3674 that was to accompany that application.

If you have already submitted the certification for this application, please disregard the above.

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Gastroenterology and Inborn Errors Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

If you have any questions, call me at (301) 796-0846.

Sincerely,

{See appended electronic signature page}

Jagjit Grewal, M.P.H.
Senior Regulatory Health Project Manager
Division of Gastroenterology and Inborn
Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

JAGJIT S GREWAL
01/13/2012