

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

209400Orig1s000

OTHER REVIEW(S)

Labeling Review for Omeprazole Delayed-Release Orally Disintegrating Tablets *Draft Labeling*

SUBMISSION DATES:	June 2, 2017
NDA/SUBMISSION TYPE:	209400
ACTIVE INGREDIENTS:	Omeprazole, 20 mg
DOSAGE FORM	Delayed-release orally disintegrating tablet
SPONSOR:	Dexcel Pharma Technologies, Ltd. U.S. Agent: CBR International Corp. Jeanne M. Novak, Ph.D. CEO and Principal Consultant 720-746-1190
REVIEWER:	Mary R. Vienna, RN, MHA, DNDP, ODE IV
TEAM LEADER	Kevin Lorick, Ph. D., DNDP, ODE IV
REGULATORY PROJECT MANAGER	Alina Salvatore, Project Manager, DNDP, ODE IV

I. BACKGROUND

Dexcel Pharma Technologies, Ltd. (Dexcel) and its U.S. agent, CBR International Corp., submitted on September 6, 2016, an original new drug application (NDA) 209400, under Section 505(b)(2) of the Federal Food Drug and Cosmetic Act (FD&C Act). The sponsor proposes to market a strawberry-flavored delayed-release orally disintegrating tablet form of the proton pump inhibitor (PPI) omeprazole 20 mg as an over-the-counter (OTC) drug product for the treatment of frequent heartburn (occurring 2 or more times per week) in adults 18 years of age and older.

The May 23, 2017 labeling review discusses the September 6 and November 4, 2016 and May 10, 2017, labeling submissions, and includes labeling recommendations that were communicated to the sponsor on May 24, 2017. This review, the second of two, amends the May 23, 2017 labeling review. This is a review of the labeling submitted June 2, 2017 compared to the labeling reviewed on May 23, 2017.

Submitted Labeling	Representative of Following SKUs	Submission date/replaces
2-count immediate container (blister)	N/A	Revised June 2, 2017
2-count sample carton	N/A	Revised June 2, 2017
7-count immediate container (blister)	N/A	September 6, 2016
14-count immediate container (blister)	N/A	September 6, 2016
14-count inner carton (blister)	N/A	Revised June 2, 2017
14-count blister carton with "NEW DOSAGE FORM"	N/A	Revised June 2, 2017
14-count blister carton with "FDA Approved"	N/A	Revised June 2, 2017
28-count blister carton with "NEW DOSAGE FORM"	N/A	Revised June 2, 2017
28-count blister carton with "FDA Approved"	N/A	Revised June 2, 2017
42-count blister carton with "NEW DOSAGE FORM"	N/A	Revised June 2, 2017
42-count blister carton with "FDA Approved"	N/A	Revised June 2, 2017
14-count immediate container (bottle)	N/A	Revised June 2, 2017
14-count bottle carton	N/A	Revised June 2, 2017
28-count bottle carton	N/A	Revised June 2, 2017
42-count bottle carton	N/A	Revised June 2, 2017

II. REVIEWER'S COMMENTS

A. 2-count sample carton, 14-count inner carton, and 14-, 28- and 42-count outer cartons

i. Outer Carton Label Outside Drug Facts

- a. The image of the pink tablet is revised to appear as a clearer image, with translucent sparkles above the tablet. The image is no longer distorted and conforms to the “Actual size” statement that appears below the tablet.

Comment: This is acceptable.

ii. Outer Carton Drug Facts Label

The Drug Facts Label (DFL) on each label has identical content regardless of count size. The DFL changes from the previous review include the following:

a. *Warnings*

1. **“Ask a doctor or pharmacist before use if you are taking:”**
 - warfarin, clopidogrel or cilostazole (blood-thinning medicines)
 - prescription antifungal or anti-yeast medicines
 - digoxin (heart medicine)
 - diazepam (anxiety medicine)
 - tacrolimus or mycophenolate mofetil (immune system medicine)
 - prescription antiretrovirals (medicines for HIV infection)
 - methotrexate (arthritis medicine)

Comment: This is acceptable, as the revised DFL presents with the word “taking” un-bolded in compliance with 21 CFR 201.66(c)(5)(v).

2. **“Stop use and ask a doctor if:”**
 - your heartburn continues or worsens
 - you need to take this product for more than 14 days
 - you need to take more than 1 course of treatment every 4 months
 - you get diarrhea
 - you develop a rash or joint pain

Comment: This is acceptable, as the bullet “you develop rash or joint pain” is added as requested by the April 6, 2017 CBE-0 supplement request letter for the listed drug (NDA 021229).

3. Keep out of reach of children:

“Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away (1-800-222-1222).”

Comment: This is acceptable, as a period at the end of the second sentence conforms to the label of the listed drug (NDA 021229).

b. ***Directions***

The bullet format for the “**14-Day Course of Treatment**” headings is changed to be subordinate to the previous three bullets and the last bullet of the ***Directions*** section. Also, a period is added to the second sentence of the directions bullet:

- place the tablet on tongue; tablet disintegrates, with or without water. The tablets can also be swallowed whole with water.

as requested in the previous review.

Comment: This is acceptable.

c. ***Other Information***

- read the directions and warnings before use
- keep the carton. It contains important information.
- store at 20-25°C (68-77°F); keep product out of high heat and moisture

Comment: The last bullet was revised to comply with CMC review labeling recommendations and is acceptable.

d. ***Questions or comments?***

1-800-719-9260: weekdays 7:30 AM to 5:00 PM EST

Comment: The section is revised to add the recommendation that the time that the toll-free number is in operation, and is acceptable.

e. ***Other Sections/Issues***

- For all carton sizes, the Drug Facts label specifications comply with 21CFR 201.66(d).

Comment: This is acceptable.

iii. **Immediate container labels (2-, 7- and 14-count blister)**

The directions on the 2-count blister label is revised to replace the statement (b) (4) with the statement “First two doses of a 14-day course of treatment.” to accurately reflect the container count size.

Comment: This is acceptable.

B. 14-, 28- and 42-count bottle cartons**i. Outer Carton Label Outside Drug Facts**

- a. The image of the pink tablet is revised to appear as a clearer image, with translucent sparkles above the tablet. The image is no longer distorted and conforms to the “Actual size” statement that appears below the tablet.

Comment: This is acceptable.

ii. Outer Carton Drug Facts Label

See Section II.A.ii.

iii. Immediate Container (14-count bottle) Label

- a. The storage statement on the left side of the bottle label is revised to conform to the CMC review label recommendations. See Section II.A.ii.(c) for details.

Comment: This is acceptable.

III. RECOMMENDATIONS

Issue an **APPROVAL** letter to the sponsor for the submitted Omeprazole delayed release orally disintegrating tablet labeling and request final printed labeling. The final printed labeling (FPL) must be identical to the following labeling:

Submitted Labeling	Submission date
2-count immediate container (blister)	June 2, 2017
2-count sample carton	June 2, 2017
7-count immediate container (blister)	September 6, 2016
14-count immediate container (blister)	September 6, 2016
14-count inner carton (blister)	June 2, 2017
14-count blister carton with “NEW DOSAGE FORM”	June 2, 2017
14-count blister carton with “FDA Approved”	June 2, 2017

Submitted Labeling	Submission date
28-count blister carton with “NEW DOSAGE FORM”	June 2, 2017
28-count blister carton with “FDA Approved”	June 2, 2017
42-count blister carton with “NEW DOSAGE FORM”	June 2, 2017
42-count blister carton with “FDA Approved”	June 2, 2017
14-count immediate container (bottle)	June 2, 2017
14-count bottle carton	June 2, 2017
28-count bottle carton	June 2, 2017
42-count bottle carton	June 2, 2017

Please remind the sponsor to remove the “NEW DOSAGE FORM!” flag after six months of marketing.

IV. SUBMITTED LABELING

The labels on the remaining pages of this labeling review were submitted and were evaluated in this labeling review:

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

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

/s/

MARY R VIENNA
06/09/2017

KEVIN L LORICK
06/12/2017
I concur with the review and recoomendations

505(b)(2) ASSESSMENT

Application Information		
NDA # 209400	NDA Supplement #:	Efficacy Supplement Type SE-
Proprietary Name: None requested by the sponsor Established/Proper Name: omeprazole Dosage Form: delayed-release, orally disintegrating tablet Strengths: 20 mg		
Applicant: Dexcel Pharma Technologies Limited Agent for Applicant: CBR International Corp.		
Date of Receipt: September 6, 2016		
PDUFA Goal Date: July 6, 2017		Action Goal Date (if different):
RPM: Alina Salvatore		
Proposed Indication(s): Treatment of frequent heartburn (occurring 2 or more days a week) in adults age 18 years and older		

GENERAL INFORMATION

- 1) Is this application for a recombinant or biologically-derived product and/or protein or peptide product *OR* is the applicant relying on a recombinant or biologically-derived product and/or protein or peptide product to support approval of the proposed product?

YES ☐ NO ☒

If "YES" contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

**INFORMATION PROVIDED VIA RELIANCE
(LISTED DRUG OR LITERATURE)**

- 2) List the information essential to the approval of the proposed drug that is provided by reliance on our previous finding of safety and efficacy for a listed drug by reliance on published literature, or by reliance on a final OTC monograph. *(If not clearly identified by the applicant, this information can usually be derived from annotated labeling.)*

Source of information* (e.g., published literature, name of listed drug(s), OTC final drug monograph)	Information relied-upon (e.g., specific sections of the application or labeling)
NDA 021229 Prilosec OTC	FDA's previous finding of safety and efficacy

*each source of information should be listed on separate rows, however individual literature articles should not be listed separately

- 3) The bridge in a 505(b)(2) application is information to demonstrate sufficient similarity between the proposed product and the listed drug(s) or to justify reliance on information described in published literature for approval of the 505(b)(2) product. Describe in detail how the applicant bridged the proposed product to the listed drug(s) and/or published literature¹. [See also Guidance for Industry Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products.](#)

The scientific bridge is established per two bioequivalence studies conducted by the applicant. Study 150075 demonstrated that the proposed omeprazole DR orally disintegrating tablet is bioequivalent to NDA 022032 omeprazole DR tablets which is also held by Dexcel. The applicant cross-referenced their Study AA24171 from NDA 022032 which demonstrated that their omeprazole DR tablet was bioequivalent to the listed drug Prilosec OTC (NDA 021229).

RELIANCE ON PUBLISHED LITERATURE

- 4) (a) Regardless of whether the applicant has explicitly stated a reliance on published literature to support their application, is reliance on published literature necessary to support the approval of the proposed drug product (i.e., the application *cannot* be approved as labeled without the published literature)?

YES ☐ NO ☒

If "NO," proceed to question #5.

- (b) Does any of the published literature necessary to support approval identify a specific (e.g., brand name) *listed* drug product?

YES ☐ NO ☐

If "NO," proceed to question #5.

If "YES," list the listed drug(s) identified by name and answer question #4(c).

- (c) Are the drug product(s) listed in (b) identified by the applicant as the listed drug(s)?

YES ☐ NO ☐

RELIANCE ON LISTED DRUG(S)

Reliance on published literature which identifies a specific approved (listed) drug constitutes reliance on that listed drug. Please answer questions #5-9 accordingly.

- 5) Regardless of whether the applicant has explicitly cited reliance on listed drug(s), does the application **rely** on the finding of safety and effectiveness for one or more listed drugs (approved drugs) to support the approval of the proposed drug product (i.e., the application cannot be approved without this reliance)?

YES ☒ NO ☐

If “NO,” proceed to question #10.

- 6) Name of listed drug(s) relied upon, and the NDA #(s). Please indicate if the applicant explicitly identified the product as being relied upon (see note below):

Name of Listed Drug	NDA #	Did applicant specify reliance on the product? (Y/N)
Prilosec OTC	021229	Y

Applicants should specify reliance on the 356h, in the cover letter, and/or with their patent certification/statement. If you believe there is reliance on a listed product that has not been explicitly identified as such by the applicant, please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

- 7) If this is a (b)(2) supplement to an original (b)(2) application, does the supplement rely upon the same listed drug(s) as the original (b)(2) application?

N/A ☒ YES ☐ NO ☐

If this application is a (b)(2) supplement to an original (b)(1) application or not a supplemental application, answer “N/A”.

If “NO”, please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

- 8) Were any of the listed drug(s) relied upon for this application:

- a) Approved in a 505(b)(2) application?

YES ☐ NO ☒

If “YES”, please list which drug(s).

Name of drug(s) approved in a 505(b)(2) application:

- b) Approved by the DESI process?

YES ☐ NO ☒

If “YES”, please list which drug(s).

Name of drug(s) approved via the DESI process:

- c) Described in a final OTC drug monograph?

YES ☐ NO ☒

If “YES”, please list which drug(s).

Name of drug(s) described in a final OTC drug monograph:

d) Discontinued from marketing?

YES ☐ NO ☒

If “**YES**”, please list which drug(s) and answer question d) i. below.

If “**NO**”, proceed to question #9.

Name of drug(s) discontinued from marketing:

i) Were the products discontinued for reasons related to safety or effectiveness?

YES ☐ NO ☐

(Information regarding whether a drug has been discontinued from marketing for reasons of safety or effectiveness may be available in the Orange Book. Refer to section 1.11 for an explanation, and section 6.1 for the list of discontinued drugs. If a determination of the reason for discontinuation has not been published in the Federal Register (and noted in the Orange Book), you will need to research the archive file and/or consult with the review team. Do not rely solely on any statements made by the sponsor.)

9) Describe the change from the listed drug(s) relied upon to support this (b)(2) application (for example, “This application provides for a new indication, otitis media” or “This application provides for a change in dosage form, from capsule to solution”).

- This application provides for a change in dosage form, from a DR tablet (Prilosec OTC) to a DR orally disintegrating tablet. Also, the proposed product contains omeprazole as the active ingredient whereas Prilosec OTC contains omeprazole magnesium.

The purpose of the following two questions is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval that should be referenced as a listed drug in the pending application.

*The assessment of pharmaceutical equivalence for a recombinant or biologically-derived product and/or protein or peptide product is complex. If you answered **YES to question #1**, proceed to question #12; if you answered **NO to question #1**, proceed to question #10 below.*

10) (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved (via an NDA or ANDA)?

*(**Pharmaceutical equivalents** are drug products in identical dosage forms intended for the same route of administration that: **(1)** contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; **(2)** do not necessarily contain the same inactive ingredients; **and (3)** meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c), FDA’s “Approved Drug Products with Therapeutic Equivalence Evaluations” (the Orange Book)).*

***Note** that for proposed combinations of one or more previously approved drugs, a pharmaceutical equivalent must also be a combination of the same drugs.*

YES ☐ NO ☒

*If “NO” to (a) proceed to question #11.
If “YES” to (a), answer (b) and (c) then proceed to question #12.*

(b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval?

YES ☐ NO ☐

(c) Is the listed drug(s) referenced by the application a pharmaceutical equivalent?

N/A ☐ YES ☐ NO ☐

*If this application relies only on non product-specific published literature, answer “N/A”
If “YES” to (c) and there are no additional pharmaceutical equivalents listed, proceed to question #12.*

If “NO” or if there are additional pharmaceutical equivalents that are not referenced by the application, list the NDA pharmaceutical equivalent(s); you do not have to individually list all of the products approved as ANDAs, but please note below if approved approved generics are listed in the Orange Book. Please also contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

Pharmaceutical equivalent(s): N/A

11) (a) Is there a pharmaceutical alternative(s) already approved (via an NDA or ANDA)?

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

***Note** that for proposed combinations of one or more previously approved drugs, a pharmaceutical alternative must also be a combination of the same drugs.*

YES ☒ NO ☐

If “NO”, proceed to question #12.

(b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval?

YES ☒ NO ☐

Note: There is one OTC pharmaceutical alternative approved for the same indication.
There are other pharmaceutical alternatives available for prescription use.

(c) Is the approved pharmaceutical alternative(s) referenced as the listed drug(s)?

N/A ☐ YES ☐ NO ☒

If this application relies only on non product-specific published literature, answer “N/A”

If “**YES**” and there are no additional pharmaceutical alternatives listed, proceed to question #12.

If “**NO**” or if there are additional pharmaceutical alternatives that are not referenced by the application, list the NDA pharmaceutical alternative(s); you do not have to individually list all of the products approved as ANDAs, but please note below if approved generics are listed in the Orange Book. Please also contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

Pharmaceutical alternative(s): NDA 022032 omeprazole DR tablet (OTC) for which Dexcel is the application holder. There are 14 ANDAs for prescription omeprazole listed in the Orange Book.

PATENT CERTIFICATION/STATEMENTS

- 12) List the patent numbers of all unexpired patents listed in the Orange Book for the listed drug(s) for which our finding of safety and effectiveness is relied upon to support approval of the (b)(2) product.

Listed drug/Patent number(s): NDA 021229 Prilosec OTC – 6403616, 6428810

No patents listed ☐ proceed to question #14

- 13) Did the applicant address (with an appropriate certification or statement) all of the unexpired patents listed in the Orange Book for the listed drug(s) relied upon to support approval of the (b)(2) product?

YES ☒ NO ☐

If “**NO**”, list which patents (and which listed drugs) were not addressed by the applicant.

Listed drug/Patent number(s):

- 14) Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

☐ No patent certifications are required (e.g., because application is based solely on published literature that does not cite a specific innovator product)

☐ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)

☒ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)

Patent number(s): 5817338, 5900424

Expiry Date: October 6, 2015; May 4, 2016

☐ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)

Patent number(s):

Expiry date(s):

- ☒ 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification). *If Paragraph IV certification was submitted, proceed to question #15.*
- ☐ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the NDA holder/patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above). *If the applicant has a licensing agreement with the NDA holder/patent owner, proceed to question #15.*
- ☐ 21 CFR 314.50(i)(1)(ii): No relevant patents.
- ☐ 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)

Patent number(s):

Method(s) of Use/Code(s):

15) Complete the following checklist **ONLY** for applications containing Paragraph IV certification and/or applications in which the applicant and patent holder have a licensing agreement:

(a) Patent number(s): 6403616, 6428810

(b) Did the applicant submit a signed certification stating that the NDA holder and patent owner(s) were notified that this b(2) application was filed [21 CFR 314.52(b)]?

YES ☒ NO

If "NO", please contact the applicant and request the signed certification.

(c) Did the applicant submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]? This is generally provided in the form of a registered mail receipt.

YES ☒ NO ☐

If "NO", please contact the applicant and request the documentation.

(d) What is/are the date(s) on the registered mail receipt(s) (i.e., the date(s) the NDA holder and patent owner(s) received notification):

Date(s): 11/29/2016

Note, the date(s) entered should be the date the notification occurred (i.e., delivery date(s)), not the date of the submission in which proof of notification was provided

(e) Has the applicant been sued for patent infringement within 45-days of receipt of the notification listed above?

***Note** that you may need to call the applicant (after 45 days of receipt of the notification) to verify this information **UNLESS** the applicant provided a written statement from the notified patent owner(s) that it consents to an immediate effective date of approval.*

YES ☐ NO ☒ Patent owner(s) consent(s) to an immediate effective date of approval ☐

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

/s/

ALINA W SALVATORE
06/22/2017

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data)]

Application Information		
NDA # 209400	NDA Supplement #: S- N/A	Efficacy Supplement Category: ☐ New Indication (SE1) ☐ New Dosing Regimen (SE2) ☐ New Route Of Administration (SE3) ☐ Comparative Efficacy Claim (SE4) ☐ New Patient Population (SE5) ☐ Rx To OTC Switch (SE6) ☐ Accelerated Approval Confirmatory Study (SE7) ☐ Labeling Change With Clinical Data (SE8) ☐ Manufacturing Change With Clinical Data (SE9) ☐ Animal Rule Confirmatory Study (SE10)
Proprietary Name: TBD/Proprietary Name Review Request not submitted by Sponsor Established/Proper Name: omeprazole Dosage Form: delayed-release, orally disintegrating tablet Strengths: 20 mg		
Applicant: Dexcel Pharma Technologies, Ltd. Agent for Applicant (if applicable): CBR International Corp		
Date of Application: 09/06/16 Date of Receipt: 09/06/16 Date clock started after Unacceptable for Filing (UN): N/A		
PDUFA Goal Date: 07/06/17		Action Goal Date (if different): N/A
Filing Date: 11/05/16		Date of Filing Meeting: 10/25/16
Chemical Classification (original NDAs only) : ☐ Type 1- New Molecular Entity (NME); NME and New Combination ☐ Type 2- New Active Ingredient; New Active Ingredient and New Dosage Form; New Active Ingredient and New Combination ☐ Type 3- New Dosage Form; New Dosage Form and New Combination ☐ Type 4- New Combination ☒ Type 5- New Formulation or New Manufacturer ☐ Type 7- Drug Already Marketed without Approved NDA ☐ Type 8- Partial Rx to OTC Switch ☐ Type 9-New Indication or Claim (will <u>not</u> be marketed as a separate NDA after approval) ☐ Type 10-New Indication or Claim (will be marketed as a separate NDA after approval)		
Proposed indication(s)/Proposed change(s): Treatment of frequent heartburn (occurs 2 or more days a week) in adults age 18 years and older.		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:		☐ 505(b)(1) ☒ 505(b)(2) ☐ 505(b)(1) ☐ 505(b)(2)
<i>If 505(b)(2)NDA/NDA Supplement: Draft the “505(b)(2) Assessment” review found at:</i> http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499 .		

Type of BLA	☐ 351(a) ☐ 351(k)
If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team	
Review Classification: The application will be a priority review if: • A complete response to a pediatric Written Request (WR) was included (a partial response to a WR that is sufficient to change the labeling should also be a priority review – check with DPMH) • The product is a Qualified Infectious Disease Product (QIDP) • A Tropical Disease Priority Review Voucher was submitted • A Pediatric Rare Disease Priority Review Voucher was submitted	☒ Standard ☐ Priority ☐ Pediatric WR ☐ QIDP ☐ Tropical Disease Priority Review Voucher ☐ Pediatric Rare Disease Priority Review Voucher
Resubmission after withdrawal? ☐	Resubmission after refuse to file? ☐
Part 3 Combination Product? ☐ If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults	☐ Convenience kit/Co-package ☐ Pre-filled drug delivery device/system (syringe, patch, etc.) ☐ Pre-filled biologic delivery device/system (syringe, patch, etc.) ☐ Device coated/impregnated/combined with drug ☐ Device coated/impregnated/combined with biologic ☐ Separate products requiring cross-labeling ☐ Drug/Biologic ☐ Possible combination based on cross-labeling of separate products ☐ Other (drug/device/biological product)

☐ Fast Track Designation ☐ Breakthrough Therapy Designation <i>(set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)</i> ☐ Rolling Review ☐ Orphan Designation ☐ Rx-to-OTC switch, Full ☐ Rx-to-OTC switch, Partial ☒ Direct-to-OTC Other:	☐ PMC response ☐ PMR response: ☐ FDAAA [505(o)] ☐ PREA deferred pediatric studies (FDCA Section 505B) ☐ Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) ☐ Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)			
Collaborative Review Division (if OTC product): DGIEP				
List referenced IND Number(s): PIND 127169				
Goal Dates/Product Names/Classification Properties	YES	NO	NA	Comment
PDUFA/BsUFA and Action Goal dates correct in the electronic archive? If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.	☒	☐		
Are the established/proper and applicant names correct in electronic archive? If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name	☒	☐		

to the supporting IND(s) if not already entered into electronic archive.					
Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, orphan drug)? <i>Check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at:</i> http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm <i>If no, ask the document room staff to make the appropriate entries.</i>		☒	☐	☐	
Application Integrity Policy		YES	NO	NA	Comment
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at:</i> http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm		☐	☒		
If yes, explain in comment column.					
If affected by AIP, has OC been notified of the submission? If yes, date notified:		☐	☐		
User Fees		YES	NO	NA	Comment
Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?		☒	☐		
User Fee Status <i>If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period from receipt. Review stops. Contact the User Fee Staff. If appropriate, send UN letter.</i>		Payment for this application (check daily email from UserFeeAR@fda.hhs.gov): ☒ Paid ☐ Exempt (orphan, government) ☐ Waived (e.g., small business, public health) ☐ Not required			
<i>If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Contact the User Fee Staff. If appropriate, send UN letter.</i>		Payment of other user fees: ☒ Not in arrears ☐ In arrears			
User Fee Bundling Policy <i>Refer to the guidance for industry, Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees at:</i> http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf		Has the user fee bundling policy been appropriately applied? <i>If no, or you are not sure, consult the User Fee Staff.</i> ☒ Yes ☐ No			
505(b)(2) (NDAs/NDA Efficacy Supplements only)		YES	NO	NA	Comment
Is the application a 505(b)(2) NDA? (Check the 356h form,		☒	☐		

cover letter, and annotated labeling). If yes , answer the bulleted questions below:																					
• Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?		☐	☒																		
• Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? [see 21 CFR 314.54(b)(1)].		☐	☒																		
• Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug [see 21 CFR 314.54(b)(2)]?		☐	☒																		
<i>If you answered yes to any of the above bulleted questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs for advice.</i>																					
• Is there unexpired exclusivity on another listed drug product containing the same active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? Check the Electronic Orange Book at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm		☐	☒																		
If yes, please list below: <table border="1"> <thead> <tr> <th>Application No.</th> <th>Drug Name</th> <th>Exclusivity Code</th> <th>Exclusivity Expiration</th> </tr> </thead> <tbody> <tr><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td></tr> </tbody> </table>						Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration												
Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration																		
<i>If there is unexpired, 5-year exclusivity remaining on another listed drug product containing the same active moiety, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2). Unexpired orphan or 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.</i>																					
Exclusivity	YES	NO	NA	Comment																	
Does another product (same active moiety) have orphan exclusivity for the same indication? Check the Orphan Drug Designations and Approvals list at: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm	☐	☒																			
If another product has orphan exclusivity , is the product considered to be the same product according to the orphan drug definition of sameness [see 21 CFR 316.3(b)(13)]?	☐	☐	☒																		
<i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy</i>																					
NDAs/NDA efficacy supplements only: Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity?	☐	☒	☐																		
If yes, # years requested:																					
Note: An applicant can receive exclusivity without requesting it;																					

<i>therefore, requesting exclusivity is not required.</i>				
NDAs only: Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use?	☐	☒	☐	
If yes, did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)? <i>If yes, contact the Orange Book Staff (CDER-Orange Book Staff).</i>	☐	☐	☒	
BLAs only: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act? <i>If yes, notify Marlene Schultz-DePalo, CDER Purple Book Manager</i> <i>Note: Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>	☐	☐	☒	

Format and Content				
<i>Do not check mixed submission if the only electronic component is the content of labeling (COL).</i>	☐ All paper (except for COL) ☒ All electronic ☐ Mixed (paper/electronic) ☒ CTD ☐ Non-CTD ☐ Mixed (CTD/non-CTD)			
If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?				
Overall Format/Content	YES	NO	NA	Comment
If electronic submission, does it follow the eCTD guidance? ¹ If not, explain (e.g., waiver granted).	☒	☐	☐	
Index: Does the submission contain an accurate comprehensive index?	☒	☐		
Is the submission complete as required under 21 CFR 314.50 (NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including: ☒ legible	☒	☐		

¹ <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm333969.pdf>

☒ English (or translated into English) ☒ pagination ☒ navigable hyperlinks (electronic submissions only)				
If no, explain.				
BLAs only: Companion application received if a shared or divided manufacturing arrangement?	☐	☐	☐	
If yes, BLA #				
Forms and Certifications				
<i>Electronic forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, <u>paper</u> forms and certifications with hand-written signatures must be included.</i> Forms include: user fee cover sheet (3397/3792), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.				
Application Form	YES	NO	NA	Comment
Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)?	☒	☐		
<i>If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].</i>				
Are all establishments and their registration numbers listed on the form/attached to the form?	☒	☐	☐	
Patent Information (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	☒	☐	☐	
Financial Disclosure	YES	NO	NA	Comment
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)?	☒	☐		
<i>Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].</i>				
<i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i>				
Clinical Trials Database	YES	NO	NA	Comment
Is form FDA 3674 included with authorized signature?	☒	☐		
<i>If yes, ensure that the application is also coded with the supporting document category, “Form 3674.”</i>				
<i>If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant</i>				

Debarment Certification	YES	NO	NA	Comment
Is a correctly worded Debarment Certification included with authorized signature? <i>Certification is not required for supplements if submitted in the original application; If foreign applicant, <u>both</u> the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].</i> <i>Note: Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e., “[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.” Applicant may not use wording such as, “To the best of my knowledge...”</i>	☒	☐	☐	
Field Copy Certification (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included? <i>Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)</i> <i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i>	☐	☐	☒	
Controlled Substance/Product with Abuse Potential	YES	NO	NA	Comment
<u>For NMEs:</u> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)? <i>If yes, date consult sent to the Controlled Substance Staff:</i> <u>For non-NMEs:</u> <i>Date of consult sent to Controlled Substance Staff:</i>	☐	☐	☒	
Pediatrics	YES	NO	NA	Comment
<u>PREA</u> Does the application trigger PREA? <i>If yes, notify PeRC@fda.hhs.gov to schedule required PeRC meeting²</i>	☒	☐		PeRC review scheduled on June 7, 2017

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027829.htm>

Version: 4/12/2016

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Note: NDAs/BLAs/efficacy supplements for new active ingredients (including new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.				
If the application triggers PREA , is there an agreed Initial Pediatric Study Plan (iPSP)? <i>If no, may be an RTF issue - contact DPMH for advice.</i>	☒	☐	☐	Full Waiver requested and agreed upon.
If required by the agreed iPSP , are the pediatric studies outlined in the agreed iPSP completed and included in the application? <i>If no, may be an RTF issue - contact DPMH for advice.</i>	☐	☐	☒	
BPCA: Is this submission a complete response to a pediatric Written Request? <i>If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required³)</i>	☐	☒		
Proprietary Name	YES	NO	NA	Comment
Is a proposed proprietary name submitted? <i>If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."</i>	☐	☒	☐	
REMS	YES	NO	NA	Comment
Is a REMS submitted? <i>If yes, send consult to OSE/DRISK and notify OC/OSI/DSC/PMSB via the CDER OSI RMP mailbox</i>	☐	☐	☒	
Prescription Labeling	☒ Not applicable			
Check all types of labeling submitted.	☐ Package Insert (Prescribing Information)(PI) ☐ Patient Package Insert (PPI) ☐ Instructions for Use (IFU) ☐ Medication Guide (MedGuide) ☐ Carton labeling ☐ Immediate container labels ☐ Diluent labeling ☐ Other (specify)			
	YES	NO	NA	Comment
Is Electronic Content of Labeling (COL) submitted in SPL format? <i>If no, request applicant to submit SPL before the filing date.</i>	☐	☐		
Is the PI submitted in Physician Labeling Rule (PLR)	☐	☐		

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027837.htm>

format? ⁴				
If PI not submitted in PLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.</i>	☐	☐	☒	
For applications submitted on or after June 30, 2015: Is the PI submitted in Pregnancy and Lactation Labeling Rule (PLLR) format? Has a review of the available pregnancy, lactation, and females and males of reproductive potential data (if applicable) been included?	☐ ☐	☐ ☐	☒ ☒	
For applications submitted on or after June 30, 2015: If PI not submitted in PLLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLLR format before the filing date.</i>	☐	☐	☒	
Has all labeling [(PI, patient labeling (PPI, MedGuide, IFU), carton and immediate container labeling)] been consulted to OPDP?	☐	☐	☒	
Has PI and patient labeling (PPI, MedGuide, IFU) been consulted to OSE/DRISK? (send WORD version if available)	☐	☐	☒	
Has all labeling [PI, patient labeling (PPI, MedGuide, IFU) carton and immediate container labeling, PI, PPI been consulted/sent to OSE/DMEPA and appropriate CMC review office in OPQ (OBP or ONDP)?	☐	☐	☒	
OTC Labeling	☐ Not Applicable			
Check all types of labeling submitted.	☒ Outer carton label ☒ Immediate container label ☒ Blister card ☒ Blister backing label ☒ Consumer Information Leaflet (CIL) ☒ Physician sample ☐ Consumer sample ☐ Other (specify)			
	YES	NO	NA	Comment
Is electronic content of labeling (COL) submitted?	☒	☐		

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/LabelingDevelopmentTeam/ucm025576.htm>

<i>If no, request in 74-day letter.</i>				
Are annotated specifications submitted for all stock keeping units (SKUs)?	☒	☐	☐	
<i>If no, request in 74-day letter.</i>				
If representative labeling is submitted, are all represented SKUs defined?	☐	☐	☒	
<i>If no, request in 74-day letter.</i>				
All labeling/packaging sent to OSE/DMEPA?	☐	☒	☐	DMEPA review not necessary
Other Consults	YES	NO	NA	Comment
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team)	☐	☒	☐	
<i>If yes, specify consult(s) and date(s) sent:</i>				
Meeting Minutes/SPAs	YES	NO	NA	Comment
End-of Phase 2 meeting(s)? Date(s):	☐	☒		Pre-IND Type B mtg held Oct 6, 2015
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? Date(s): May 9, 2016	☒	☐		
Any Special Protocol Assessments (SPAs)? Date(s):	☐	X		

ATTACHMENT

MEMO OF FILING MEETING

DATE: October 25, 2016

BACKGROUND: Pre-IND Type B meeting held with sponsor on October 6, 2015.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Alina Salvatore	Y
	CPMS/TL:	Dan Brum	Y
Cross-Discipline Team Leader (CDTL)	Francis Becker		Y
Division Director/Deputy	Karen Mahoney		Y
Office Director/Deputy	Theresa Michele		N
Clinical	Reviewer:	Ryan Raffaelli	Y
	TL:	Francis Becker	Y
Social Scientist Review (<i>for OTC products</i>)	Reviewer:		
	TL:		
OTC Labeling Review (<i>for OTC products</i>)	Reviewer:	Mary Vienna	Y
	TL:	Kevin Lorick	Y
Clinical Microbiology (<i>for antimicrobial products</i>)	Reviewer:		
	TL:		
Clinical Pharmacology	Reviewer:	Sandhaya Apparaju	Y
	TL:	Sue Chih Lee	Y
• Genomics	Reviewer:		
• Pharmacometrics	Reviewer:		
Biostatistics	Reviewer:		
	TL:		

Nonclinical (Pharmacology/Toxicology)	Reviewer:	Charlie Donald Thompson	Y
	TL:	Jane Sohn	Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Product Quality (CMC) Review Team:	ATL:	Swapan De	Y
	RBPM:	Thao Vu	Y
• Drug Substance	Reviewer:	Friedrich Burnett	Y
• Drug Product	Reviewer:	Elise Luong	Y
• Process	Reviewer:	Krishnaiah Yellela	Y
• Microbiology	Reviewer:		
• Facility	Reviewer:	Carl Lee	Y
• Biopharmaceutics	Reviewer:	Hansong Chen	Y
• Immunogenicity	Reviewer:		
• Labeling (BLAs only)	Reviewer:		
• Other (e.g., Branch Chiefs, EA Reviewer)	Danae Christodoulou		N
OMP/OMPI/DMPP (MedGuide, PPI, IFU)	Reviewer:		
	TL:		
OMP/OPDP (PI, PPI, MedGuide, IFU, carton and immediate container labeling)	Reviewer:		
	TL:		
OSE/DMEPA (proprietary name, carton/container labeling)	Reviewer:		
	TL:		
OSE/DRISK (REMS)	Reviewer:		
	TL:		
OC/OSI/DSC/PMSB (REMS)	Reviewer:		
	TL:		

Bioresearch Monitoring (OSI)	Reviewer:		
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers/disciplines			
Discipline (DGEIP Clinical) *For additional lines, highlight this group of cells, copy, then paste: select "insert as new rows"	Reviewer:	Marjorie Dannis	N
	TL:	Anil Rajpal	N
Other attendees	Jagjit Grewal		Y
	Betsy Scroggs		Y
	*For additional lines, right click here and select "insert rows below"		

FILING MEETING DISCUSSION:

GENERAL 505(b)(2) filing issues: - Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? - Did the applicant provide a scientific "bridge" demonstrating the relationship between the proposed product and the referenced product(s)/published literature? Describe the scientific bridge (e.g., information to demonstrate sufficient similarity between the proposed product and the listed drug(s) such as BA/BE studies or to justify reliance on information described in published literature):		☐ Not Applicable ☐ YES ☒ NO ☒ YES ☐ NO The scientific bridge is established per two bioequivalence studies conducted by the applicant. Study 150075 demonstrated that the proposed omeprazole DR orally disintegrating tablet is bioequivalent to NDA 022032 omeprazole DR tablets which is also held by Dexcel. The applicant cross-referenced their Study AA24171 from NDA 022032 which demonstrated that their omeprazole DR tablet was bioequivalent to the listed
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	drug Prilosec OTC (NDA 021229).
Per reviewers, are all parts in English or English translation? If no, explain:	☒ YES ☐ NO
Electronic Submission comments List comments:	☐ Not Applicable ☒ No comments

CLINICAL Comments:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☒ Review issues for 74-day letter
Clinical study site(s) inspections(s) needed? If no, explain:	☒ YES ☐ NO
- Advisory Committee Meeting needed? Comments: <i>If no, for an NME NDA or original BLA, include the reason. For example:</i> <i>this drug/biologic is not the first in its class</i> <i>the clinical study design was acceptable</i> <i>the application did not raise significant safety or efficacy issues</i> <i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i>	☐ YES Date if known: ☒ NO ☐ To be determined Reason:
If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? Comments:	☒ Not Applicable ☐ YES ☐ NO
CONTROLLED SUBSTANCE STAFF Abuse Liability/Potential Comments:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CLINICAL MICROBIOLOGY Comments:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter

CLINICAL PHARMACOLOGY Comments:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
Clinical pharmacology study site(s) inspections(s) needed?	☐ YES ☒ NO
BIOSTATISTICS Comments:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
NONCLINICAL (PHARMACOLOGY/TOXICOLOGY) Comments:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
PRODUCT QUALITY (CMC) Comments:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☒ Review issues for 74-day letter
<u>New Molecular Entity (NDAs only)</u> Is the product an NME?	☐ YES ☒ NO
<u>Environmental Assessment</u> Categorical exclusion for environmental assessment (EA) requested? If no, was a complete EA submitted? Comments:	☒ YES ☐ NO ☐ YES ☐ NO
<u>Facility Inspection</u> Establishment(s) ready for inspection? Comments:	☐ Not Applicable ☒ YES ☐ NO

<u>Facility/Microbiology Review (BLAs only)</u> Comments:	☐ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
<u>CMC Labeling Review (BLAs only)</u> Comments:	☐ Review issues for 74-day letter
<u>APPLICATIONS IN THE PROGRAM (PDUFA V)</u> (NME NDAs/Original BLAs) • Were there agreements made at the application's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application? • If so, were the late submission components all submitted within 30 days?	☐ N/A ☐ YES ☐ NO ☐ YES ☐ NO
• What late submission components, if any, arrived after 30 days?	
• Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?	☐ YES ☐ NO
• Is a comprehensive and readily located list of all clinical sites included or referenced in the application?	☐ YES ☐ NO
• Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?	☐ YES ☐ NO

REGULATORY PROJECT MANAGEMENT	
Signatory Authority: Karen Mahoney Date of Mid-Cycle Meeting (for NME NDAs/BLAs in “the Program” PDUFA V): 21st Century Review Milestones (see attached) (listing review milestones in this document is optional): Comments:	
REGULATORY CONCLUSIONS/DEFICIENCIES	
☐	The application is unsuitable for filing. Explain why:
☒	The application, on its face, appears to be suitable for filing. <u>Review Issues:</u> ☐ No review issues have been identified for the 74-day letter. ☒ Review issues have been identified for the 74-day letter. <u>Review Classification:</u> ☒ Standard Review ☐ Priority Review
ACTION ITEMS	
☒	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into the electronic archive (e.g., chemical classification, combination product classification, orphan drug).
☐	If RTF, notify everyone who already received a consult request, OSE PM, and RBPM
☐	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
☐	If priority review, notify applicant in writing by day 60 (see CST for choices)
☒	Send review issues/no review issues by day 74
☐	Conduct a PLR format labeling review and include labeling issues in the 74-day letter
☐	Update the PDUFA V DARRTS page (for applications in the Program)
☐	Other

Annual review of template by OND ADRA completed: April 2016

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

/s/

ALINA W SALVATORE
06/02/2017

Labeling Review for Omeprazole Delayed-Release Orally Disintegrating Tablets *Draft Labeling*

SUBMISSION DATES:	September 6, 2016 November 4, 2016 May 10, 2017
NDA/SUBMISSION TYPE:	209400
ACTIVE INGREDIENTS:	Omeprazole, 20 mg
DOSAGE FORM	Delayed-release orally disintegrating tablet
SPONSOR:	Dexcel Pharma Technologies, Ltd. U.S. Agent: CBR International Corp. Jeanne M. Novak, Ph.D. CEO and Principal Consultant 720-746-1190
REVIEWER:	Mary R. Vienna, RN, MHA, DNDP, ODE IV
TEAM LEADER	Kevin Lorick, Ph. D., DNDP, ODE IV
REGULATORY PROJECT MANAGER	Alina Salvatore, Project Manager, DNDP, ODE IV

I. BACKGROUND

Dexcel Pharma Technologies, Ltd. (Dexcel) and its U.S. agent, CBR International Corp., submitted on September 6, 2016, an original new drug application (NDA) 209400, under Section 505(b)(2) of the Federal Food Drug and Cosmetic Act (FD&C Act). The sponsor proposes to market a strawberry-flavored delayed-release orally disintegrating tablet form of the proton pump inhibitor (PPI) omeprazole 20 mg as an over-the-counter (OTC) drug product for the treatment of frequent heartburn (occurring 2 or more times per week) in adults 18 years of age and older. Although a delayed-release tablet form of omeprazole 20 mg is currently approved as

an OTC drug product in NDA 022032, the listed drug for safety and efficacy data is NDA 021229 (Prilosec OTC), which is a salt form of the drug (omeprazole magnesium, 20.6mg, equivalent to 20 mg omeprazole). For Drug Facts labeling review purposes, two other approved applications will be used for comparison: NDA 022032 (omeprazole 20mg) for the **Active ingredient** section of the Drug Facts label because the active ingredients are identical; and NDA 208025 (lansoprazole 15mg) for aspects of the **Directions** section of the proposed label unique to the orally disintegrating tablet dosage form, as NDA 208025 is the only approved OTC PPI with the orally disintegrating tablet dosage form.

The application was filed and an information request was sent to the sponsor on October 26, 2016, requesting clarification on the submitted labeling and corrections of errors in the labeling summary, specifications for the Drug Facts label and label identifications. The sponsor responded on November 4, 2016 with the requested corrections, withdrew 29 of the submitted labels and revised 5 of the submitted labels. A second information request was sent on April 26, 2017 requesting the re-submission of two bottle carton labels with missing information when printed, and a request for samples of tablets with a proposed carton label to verify the tablet image and “Actual size” labeling claim. The sponsor responded on May 10, 2017 with the requested labels plus three others with identified printing problems, as well as the requested tablets and carton.

The submitted labeling is compared to the most recently approved labeling of the listed drug for this application, Prilosec OTC tablets, 20 mg (NDA 021229, S-026).

Submitted Labeling	Representative of Following SKUs	Submission date/replaces
2-count immediate container (blister)	N/A	September 6, 2016
7-count immediate container (blister)	N/A	September 6, 2016
14-count immediate container (blister)	N/A	September 6, 2016
14-count immediate container (bottle)	N/A	September 6, 2016 Revised November 4, 2016
(b) (4)		
14-count inner carton (version 2) (blister)	N/A	September 6, 2016
2-count sample carton	N/A	September 6, 2016 Revised November 4, 2016 Revised May 10, 2017
(b) (4)		

Submitted Labeling	Representative of Following SKUs	Submission date/replaces
14-count carton (bottle)	N/A	September 6, 2016 Revised November 4, 2016 Revised May 10, 2017
(b) (4)		
14-count blister carton with "FDA Approved" (version 2)	N/A	September 6, 2016
14-count blister carton with "NEW DOSAGE FORM"	N/A	September 6, 2016 Revised May 10, 2017
(b) (4)		
28-count bottle carton	N/A	September 6, 2016 Revised November 4, 2016 Revised May 10, 2017
(b) (4)		
28-count blister carton with "FDA Approved" (version 2)	N/A	September 6, 2016
(b) (4)		
(b) (4)		
28-count blister carton with "NEW DOSAGE FORM"	N/A	September 6, 2016
(b) (4)		
42-count bottle carton	N/A	September 6, 2016 Revised November 4, 2016 Revised May 10, 2017
(b) (4)		

Submitted Labeling	Representative of Following SKUs	Submission date/replaces
42-count blister carton with "FDA Approved" (version 2)	N/A	September 6, 2016
(b) (4)		
(b) (4)		

Submitted Labeling	Representative of Following SKUs	Submission date/replaces
 (b) (4)		
42-count blister carton with "NEW DOSAGE FORM"	N/A	September 6, 2016

II. REVIEWER'S COMMENTS

A. 2-count sample carton, 14-count inner carton, and 14-, 28- and 42-count outer cartons

i. Outer Carton Label Outside Drug Facts

Principal Display Panel

- a. The principal display panel (PDP) has a pink-purple background with the statement of identity "Omeprazole Delayed Release Orally Disintegrating Tablets 20 mg Acid Reducer" in white font on the upper central portion of the PDP. There is no approved proprietary name for the drug, and one does not appear on the PDP.

Comment: This is a true statement of the "Active ingredient" and "Purpose" sections of the Drug Facts label that complies with 21 CFR 201.61 and is therefore acceptable.

- b. The statement "Treats **Frequent** Heartburn! Occurring **2 or More Days a Week**" appears in white font below the statement of identity on the PDP.

Comment: This is a true statement of the "Uses" section of the Drug Facts label and is acceptable.

- c. The declaration of net quantity of contents appears as a tablet number on the lower left section of the PDP in prominent white font.

Comment: This complies with 21 CFR 201.62 and is acceptable.

- d. For all cartons, the statement "Strawberry Flavor" appears on the right side of the PDP and for all outer cartons, a graphic image of a strawberry appears to the right of this statement.

Comment: This is acceptable.

- e. The image of a pink tablet appears on the lower right corner of the PDP with a white smear to the right of the tablet, which distorts the tablet image. The statement “Actual size” appears below the tablet.

Comment: This is not acceptable. The image of the tablet is distorted, which affects the accuracy of the “Actual size” statement. We recommend revising the graphic image to be similar to the orally disintegrating tablet graphic approved for the sponsor’s NDA 208025, S-003, approved on May 9, 2017.

- f. The statement “Orally Disintegrating Tablet” appears in white font to the left of the tablet image.

Comment: This is a truthful statement of the dosage form and is acceptable.

- g. The NDA number appears on the upper right corner of the PDP.

Comment: This complies with 21 CFR 201.2 and is acceptable.

- h. For the 14-count carton labels, the statement “One 14-day course of treatment” appears below the declaration of net quantity. For the 28-count carton labels, the statement “Two 14-day courses of treatment” appears below the declaration of net quantity. For the 42-count carton labels, the statement “Three 14-day courses of treatment” appears below the declaration of net quantity. For the 2-count sample carton, the statement “Follow samples with a 14-day course of treatment” appears below the declaration of net quantity. These statements are identical to those that appear on the 2-, 14-, 28- and 42-count cartons for the listed drug, NDA 021229.

Comment: This is acceptable.

- i. For all cartons except the 14-count inner carton, a red flag with the statement “NEW DOSAGE FORM!” appears in white font on the upper left corner of the PDP.

Comment: This is acceptable. Remind the sponsor to remove the statement after six months of marketing.

- j. For all cartons except the 14-count inner carton, a yellow flag with the statement “Melts in your mouth” appears immediately below the statement of identity. The additional statement “Dissolves without water” appears on the flag of one version of the 14-, 28 and 42-count outer cartons.

Comment: This is acceptable. “Dissolves without water” is a true statement of the “Directions” section of the Drug Facts label and the statement “Melts in your

mouth” is approved for another OTC PPI orally disintegrating tablet label (see NDA 208025, S-003).

- k. A yellow flag with the statement “FDA Approved” appears on the upper right corner of the 2-count sample carton and one version of the 14-, 28- and 42-count outer cartons.

Comment: This is acceptable.

- l. For the 2-count sample carton PDP, the statement “FREE SAMPLE INSIDE (NOT FOR SALE) with the statement “Read Drug Facts label on the back before trying” appears on the upper left corner of the PDP.

Comment: This is acceptable.

Top, side and bottom carton panels

- m. The tamper-evident feature statement “Safety Feature – Do not use if printed tablet blister unit is open or torn.” appears on the top panel of all cartons.

Comment: This is acceptable.

- n. “Tips for Managing Heartburn” appears on the bottom panel of the 2-count sample carton, 14-count inner carton and 14-count outer carton. This information appears on the top panel of the 28- and 42-count outer cartons.

Comment: This is acceptable.

- o. The country of origin statement “Made in Israel” appears on the left side panel of the 2-count sample carton, 14-count inner carton and 14-count outer carton. This information appears on the bottom panel of the 28- and 42-count outer cartons.

Comment: This is acceptable in accordance with 19 CFR 102, Rules of Origin. Defer to the CMC review regarding the acceptability of the proposed statement content.

- p. The manufacturing information “Manufactured by: Dexcel Pharma Technologies Ltd. 10 Hakidma St. Yokneam 2069200, Israel” appears directly below the country of origin statement.

Comment: This is acceptable.

- q. For the 14-count inner carton, the statement “NOT FOR RESALE” appears on the left side of the top panel.

Comment: This is acceptable.

ii. Outer Carton Drug Facts Label

The Drug Facts Label (DFL) on each label has identical content regardless of count size. The different sections include the following:

- a. **Active ingredient (in each tablet):** “Omeprazole 20 mg”

Comment: This is identical to the Omeprazole tablet DFL (NDA 022032), which has the same active ingredient and is acceptable.

- b. **Purpose:** “Acid reducer”

Comment: This is acceptable as required under 21 CFR 201.66(c)(3).

- c. **Uses:**

- treats frequent heartburn (occurs **2 or more** days a week)
- not intended for immediate relief of heartburn; this drug may take 1 to 4 days for full effect

Comment: This is identical to the DFL of the listed drug, NDA 021229, and is acceptable.

- d. **Warnings**

1. Other warnings:

“Allergy alert: Do not use if you are allergic to omeprazole”

Comment: This warning complies with 21CFR 201.66(c)(5)(ii)(B) and is acceptable.

2. **“Do not use if you have:”**

- trouble or pain swallowing food, vomiting with blood, or bloody or black stools
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**

These may be signs of a serious condition. See your doctor.

Comment: This warning is identical to the most recently approved warning for the DFL of the listed drug, NDA 021229, and is acceptable.

3. **“Ask a doctor before use if you have:”**

- had heartburn over 3 months. This may be a sign of a more serious condition.

- frequent wheezing, particularly with heartburn
- unexplained weight loss
- nausea or vomiting
- stomach pain

Comment: This warning is identical to the most recently approved warning for the DFL of the listed drug, NDA 021229, and is acceptable.

4. **“Ask a doctor or pharmacist before use if you are taking:”**
- warfarin, clopidogrel or cilostazole (blood-thinning medicines)
 - prescription antifungal or anti-yeast medicines
 - digoxin (heart medicine)
 - diazepam (anxiety medicine)
 - tacrolimus or mycophenolate mofetil (immune system medicine)
 - prescription antiretrovirals (medicines for HIV infection)
 - methotrexate (arthritis medicine)

Comment: In the warning heading, the word “taking” is bolded. 21 CFR 201.66(c)(5)(v) requires that only the language “Ask a doctor or pharmacist before use if you are” be in bold type. Revise the warning heading to unbold the word “taking” so that the warning heading reads “Ask a doctor or pharmacist before use if you are taking:”. The content of the warning is identical to the most recently approved warning for the DFL of the listed drug, NDA 021229, and is acceptable.

5. **“Stop use and ask a doctor if:”**
- your heartburn continues or worsens
 - you need to take this product for more than 14 days
 - you need to take more than 1 course of treatment every 4 months
 - you get diarrhea

Comment: This is not acceptable. Revise this warning section to add the bullet “[bullet] you develop rash or joint pain” after the bullet that reads “you get diarrhea”. (b) (4)



6. Pregnancy/breastfeeding :
- “If pregnant or breast-feeding, ask a health professional before use.”**

Comment: This statement complies with 21CFR 201.63(a) and 201.66(c)(5)(ix), and is therefore acceptable.

7. Keep out of reach of children:

“Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away (1-800-222-1222)”

Comment: To comply with the label of the listed drug (NDA 021229) revise the second sentence to add a period at the end of the sentence. The statement should read **“In case of overdose, get medical help or contact a Poison Control Center right away (1-800-222-1222).”** The statements otherwise comply with 21CFR 330.1(g) and 201.66(c)(5)(x), and are acceptable.

e. ***Directions***

1. The first three bullets state:
 - for adults 18 years of age and older
 - this product is to be used once a day (every 24 hours), every day for 14 days
 - it may take 1 to 4 days for full effect; some people get complete relief of symptoms within 24 hours

Comment: These statements are identical to the most recently approved ***Directions*** section for the DFL of the listed drug, NDA 021229, and are acceptable.

2. Under the heading **“14-Day Course of Treatment”**, the following bullets state:
 - take 1 tablet before eating in the morning
 - **do not crush or chew tablets**
 - place the tablet on tongue; tablet disintegrates, with or without water. The tablets can also be swallowed whole with water
 - take every day for 14 days
 - do not take more than 1 tablet a day
 - do not use for more than 14 days unless directed by your doctor
 - do not take this medicine with alcohol

Under the heading **“Repeated 14-Day Courses (if needed)”**, the following bullets state:

- you may repeat a 14-day course every 4 months
- **do not take for more than 14 days or more often than every 4 months unless directed by a doctor**

Comment: The directions in the **“14-Day Course of Treatment”** section differ from the DFL of the listed drug, NDA 021229, which is a tablet. However the directions are identical to those approved for an OTC PPI (NDA 208025) of the same dosage form and are therefore acceptable. Add a period after the second sentence of the third bullet so that the statement reads **“[bullet] place the tablet on tongue; tablet disintegrates, with or without water. The tablets can also be swallowed whole with**

water.” Refer to the approved DFL for NDA 208025. Also, revise the format of this section to indent both headings and the bullets under the headings to make them subordinate to the previous three bullets in the *Directions* section. Refer to the approved DFL for NDA 021229, S-026.

3. The last bullet in the *Directions* section states:
“children under 18 years of age: ask a doctor before use. Heartburn in children may sometimes be caused by a serious condition.”

Comment: This statement is identical to the DFL of the listed drug, NDA 021229, with the exception of the added text “before use” at the end of the first sentence. However, since the complete sentence is approved for other OTC PPIs (including NDA 208025), this is acceptable. Ensure that the bullet is formatted so that it is not aligned with the “14-Day Course of Treatment” and “Repeated 14-Day Courses (if needed)” sections, but is moved out to align with the first three bullets under the *Directions* section. Refer to the approved DFL for the listed drug, NDA 021229, S-026.

f. ***Other Information***

- read the directions and warnings before use
- keep the carton. It contains important information.
- store at 20-25°C (68-77°F) and protect from moisture

Comment: These are identical to the approved DFL for the listed drug, NDA 021229, and are acceptable. Defer to CMC review regarding the acceptability of the proposed storage statement.

g. ***Inactive ingredients***

The inactive ingredients are listed in alphabetical order in compliance with 21 CFR 201.66(c)(8).

Comment: This is acceptable. Defer to CMC review regarding the acceptability of inactive ingredients.

h. ***Questions or comments?***

1-800-719-9260

Comment: Recommend that the time that the toll-free number is in operation be included under this Drug Facts subheading.

i. ***Other Sections/Issues***

- For all carton sizes, the Drug Facts label specifications comply with 21CFR 201.66(d).

Comment: This is acceptable.

iii. **Immediate container labels (b) (4) 7- and 14-count blister)**

- a. The following directions appear at the top of the (b) (4) 7-count blister foil labels, and in the center of the 14-count blister foil label:

Place on tongue; tablet disintegrates, with or without water.

Do not crush or chew tablets.

One 14-day course of treatment.

Take 1 tablet every day for 14 days.

Do not take for more than 14 days or more often than every 4 months unless directed by a doctor.

Comment: The statement “One 14-day course of treatment” for the (b) (4) (b) (4) While the 14-count carton used with the 7- and 14-count blister labels does contain a 14-day course of treatment, the (b) (4)

- b. Each blister contains the following information on the push-through container:

Omeprazole
Delayed Release Orally
Disintegrating Tablets 20 mg
acid reducer
Push tablet through foil
Dexcel Pharma Technologies Ltd.
10 Hakidma St. Yokneam 2069200,
Israel

Comment: This is acceptable.

B. 14-, 28- and 42-count bottle cartons

i. Outer Carton Label Outside Drug Facts

Principal Display Panel

- a. The principal display panel (PDP) has a pink-purple background with the statement of identity “Omeprazole Delayed Release Orally Disintegrating Tablets 20 mg Acid Reducer” in white font on the upper central portion of the PDP. There is no approved proprietary name for the drug, and one does not appear on the PDP.

Comment: This is a true statement of the “*Active ingredient*” and “*Purpose*” sections of the Drug Facts label that complies with 21 CFR 201.61 and is therefore acceptable.

- b. The statement “Treats **Frequent** Heartburn! Occurring **2 or More Days a Week**” appears in white font below the statement of identity on the PDP.

Comment: This is a true statement of the “Uses” section of the Drug Facts label and is acceptable.

- c. The declaration of net quantity of contents appears as a tablet number on the lower left section of the PDP in prominent white font.

Comment: This complies with 21 CFR 201.62 and is acceptable.

- d. For the 14-count carton label, the statement “One 14-day course of treatment” appears below the declaration of net quantity. For the 28-count carton label, the statement “Two 14-day courses of treatment” appears below the declaration of net quantity. For the 42-count carton label, the statement “Three 14-day courses of treatment” appears below the declaration of net quantity.

Comment: This is acceptable.

- e. The statement “Strawberry Flavor” appears on the PDP with a graphic image of a strawberry immediately above it. For the 14-count bottle carton, this appears on the left side of the PDP, and this appears on the right side of the PDP for the 28- and 42-count bottle cartons.

Comment: This is acceptable.

- f. The image of a pink tablet appears on the lower right corner of the PDP with a white smear to the right of the tablet, which distorts the tablet image. The statement “Actual size” appears below the tablet.

Comment: This is not acceptable. The image of the tablet is distorted, which affects the accuracy of the “Actual size” statement. We recommend revising the graphic image to be similar to the orally disintegrating tablet graphic approved for the sponsor’s NDA 208025, S-003.

- g. The NDA number appears on the upper right corner of the PDP for the 14-count bottle carton, and in the upper center portion of the PDP for the 28- and 42-count bottle carton.

Comment: This complies with 21 CFR 201.2 and is acceptable.

- h. For the 14-count carton label, the statement “1 bottle inside” appears on the upper left side of the PDP. For the 28-count carton label, the statement “2 bottles inside” appears on the upper left side of the PDP. For the 42-count carton label, the statement “3 bottles inside” appears on the upper left side of the PDP.

Comment: This is acceptable.

- i. A red flag with the statement “NEW DOSAGE FORM!” appears in white font across the top of the 14-count carton PDP, and the flag appears on the upper left corner of the PDP for the 28- and 42-count cartons.

Comment: This is acceptable. Remind the sponsor to remove the statement after six months of marketing.

- j. For the 28- and 42-count cartons, a yellow flag with the statement “Melts in your mouth” appears immediately below the statement of identity.

Comment: This is acceptable. See comment under Section II.A.i.j.

- k. A yellow flag with the statement “FDA Approved” appears across the top of the 14-count carton PDP and on the upper right corner of the PDP for the 28- and 42-count cartons.

Comment: This is acceptable.

Top, side and bottom carton panels

- l. The tamper-evident feature statement “Safety Feature – Do not use if printed seal under cap is broken or missing.” appears on the left side panel of the 14- and 28-count carton, and on the right side panel of the 42-count carton.

Comment: This is acceptable.

- m. “Tips for Managing Heartburn” appears on the top panel of the 14-count, on the left side panel of the 28-count carton and on the right side panel of the 42-count cartons.

Comment: This is acceptable.

- n. The statement “Omeprazole Delayed Release Orally Disintegrating Tablets 20 mg Acid Reducer” appears on the top panel of the 28- and 42-count outer cartons.

Comment: This is acceptable.

- o. For all cartons, the manufacturing information “Manufactured by: Dexcel Pharma Technologies Ltd. 10 Hakidma St. Yokneam 2069200, Israel” appears at the bottom of the right side panel.

Comment: This is acceptable.

ii. Outer Carton Drug Facts Label

See Section II.A.ii.

iii. Immediate Container (14-count bottle) Label

- a. The principal display panel (PDP) has a pink-purple background with the statement of identity “Omeprazole Delayed Release Orally Disintegrating Tablets 20 mg Acid Reducer” in white font on the upper central portion of the PDP. There is no approved proprietary name for the drug, and one does not appear on the PDP.

Comment: This is a true statement of the “Active ingredient” and “Purpose” sections of the Drug Facts label that complies with 21 CFR 201.61 and is therefore acceptable.

- b. The statement “Treats **Frequent** Heartburn! Occurring **2 or More Days a Week**” appears in white font below the statement of identity on the PDP.

Comment: This is a true statement of the “Uses” section of the Drug Facts label and is acceptable.

- c. The declaration of net quantity of contents appears as a tablet number on the lower left section of PDP in white font.

Comment: This complies with 21 CFR 201.62 and is acceptable.

- d. The statement “Strawberry Flavor” appears on the PDP to the right of the net quantity statement.

Comment: This is acceptable.

- e. The statement “One 14-day course of treatment” appears at the bottom of the PDP.

Comment: This is acceptable.

- f. The statement “NOT FOR RESALE” appears at the top of the PDP.

Comment: This is acceptable.

- g. The manufacturing information “Manufactured by: Dexcel Pharma Technologies Ltd. 10 Hakidma St. Yokneam 2069200, Israel” appears on the right side panel of the bottle label.

Comment: This is acceptable.

- h. The tamper-evident feature statement “Safety Feature – Do not use if printed seal under cap is broken or missing.” appears on the left side panel.

Comment: This is acceptable.

- i. The statement “This label does not contain full product information. See carton for complete information. Read warnings and directions on carton before use. Retain carton for reference.” appears below the tamper evident feature statement.

Comment: This is acceptable.

- j. The *Active ingredient*, *Purpose*, *Use*, and *Other information* sections of the DFL appear on the far left side of the bottle label. See Section II.A.ii, a, b, c and f for details.

Comment: This is acceptable.

III. RECOMMENDATIONS

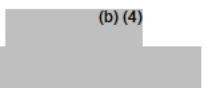
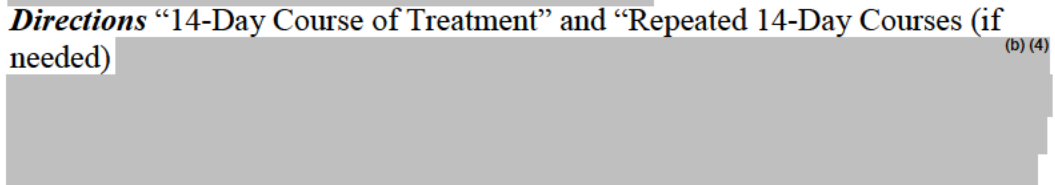
Please communicate the following to the sponsor:

A. The following revisions are to be made by the sponsor:

i. Non Drug Facts Labeling

- a.  (b) (4)
- b.  (b) (4)

ii. Drug Facts Label

- a. *Ask a doctor or pharmacist before use if you are taking:* section,  (b) (4)
- b. *Stop use and ask a doctor if:* section,  (b) (4)
- c. **Keep out of reach of children** section,  (b) (4)
- d. **Directions** “14-Day Course of Treatment” and “Repeated 14-Day Courses (if needed)”  (b) (4)

(b) (4)

- e. *Directions* “14-Day Course of Treatment” section,

(b) (4)

B. We also recommend that the sponsor make the following revisions:

i. Drug Facts label:

- a. *Questions or comments?:*

(b) (4)

Recommend that the sponsor print out draft labels and check for accuracy before submitting to ensure resolution of the technical issues with missing information on printed labels.

IV. SUBMITTED LABELING

The labels on the remaining pages of this labeling review were submitted and were evaluated in this labeling review:

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

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

/s/

MARY R VIENNA
05/23/2017

KEVIN L LORICK
05/23/2017
I concur with the review and recommendations

MEMORANDUM

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

DATE: April 10, 2017

TO: Theresa M. Michele, M.D.
Director
Division of Nonprescription Drug Products
Office of New Drugs

Dale Conner, Pharm.D.
Director (Acting)
Office of Bioequivalence
Office of Generic Drugs

FROM: Li-Hong Yeh, Ph.D.
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

THROUGH: Arindam Dasgupta, Ph.D.
Deputy Director
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: Surveillance inspection of (b) (4),
(b) (4)

Inspection Summary:

The Office of Study Integrity and Surveillance (OSIS) arranged for an inspection of in vivo bioequivalence studies (b) (4) (ANDAs (b) (4) and 150075 (NDA 209400) conducted by (b) (4). At the conclusion of the inspection, no significant issues were observed and Form FDA 483 was not issued. The final classification for this inspection is No Action Indicated (NAI).

Upon review of inspectional findings, I found the data from the clinical portion of studies (b) (4) 150075 to be reliable. Thus, I recommend that the data from all pending studies conducted by (b) (4) from 2015 to 2017 be accepted for further Agency review.

illance inspection of

(b) (4)

(b) (4)

Audited in vivo bioequivalence studies:

(b) (4)

NDA 209400

Study Number: 150075

Study Title: "Randomized, Open-Label, 4-Way Crossover Bioequivalence Study of Omeprazole Delayed-Release Orally Disintegrating Tablet 20 mg and Omeprazole Delayed-Release Tablet (Reference) Following a 20 mg Dose in Healthy Subjects under Fasting Conditions"

Dates of

Study Conduct: 11/30/2015 - 12/28/2015

ORA Investigator Karen M. Cooper (CIN-DO) conducted the clinical inspection at

(b) (4)

from

(b) (4)

. Ms. Cooper inspected the clinical facilities and equipment, reviewed personnel training program, protocols, subject records (eCRFs) and source documents, informed consent forms, adverse events reporting, subject enrollment in each study, test and reference drug accountability and retention, record retention and study communication files between the International Ethics Committee (IEC) and sponsor. At the conclusion of the inspection, Ms. Cooper did not observe any significant issues and did not issue Form FDA 483.

(b) (4)

Conclusion:

After reviewing the EIR and the inspection, I conclude that the clinical portion of Studies (b) (4) **150075** are reliable. Thus, I recommend that the data from all pending studies conducted by (b) (4) from 2015 to 2017 be accepted for further Agency review.

Li-Hong Yeh, Ph.D.
Chemical Engineer
DND/BE/OSIS

Final Classification:

Clinical site

NAI- (b) (4) (b) (4) (FEI: (b) (4))

CC:

OTS/OSIS/Kassim/Taylor/Choe/Kadavil/Turner-Rinehardt/Fenty-Stewart/Nkah/Miller/Johnson

OTS/OSIS/DND/BE/Bonapace/Dasgupta/Ayala/Biswas/Yeh

OTS/OSIS/DGDBE/Cho/Haidar/Skelly/Choi/Au

Draft: PY 04/06/2017

Edits: RCA 4/7/2017 AD 04/09/2017

ECMS: Cabinets/CDER_OC/OSI/Division of Bioequivalence & Good Laboratory Practice Compliance/INSPECTIONS/BE Program/

Clinical Sites/ (b) (4)

(b) (4)

/NDA 209400_Omeprazole

BE File #: 7304, 7310

FACTS: (b) (4)

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

/s/

LI-HONG P YEH
04/10/2017

RUBEN C AYALA
04/10/2017

ARINDAM DASGUPTA
04/10/2017

M E M O R A N D U M

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

DATE: March 9, 2017

TO: Dale P. Conner, Pharm.D.
Acting Director
Office of Bioequivalence
Office of Generic Drugs

Theresa M. Michele, M.D.
Director
Division of Nonprescription Drug Products
Office of New Drugs

Hylton V. Joffe, M.D.
Director
Division of Bone, Reproductive and Urologic Products
Office of New Drugs

FROM: Melkamu Getie-Kehtie, R.Ph., Ph.D.
Division of Generic Drug Bioequivalence Evaluation
Office of Study Integrity and Surveillance (OSIS)

Li-Hong Yeh, Ph.D.
Division of New Drug Bioequivalence Evaluation
Office of Study Integrity and Surveillance (OSIS)

THROUGH: Seongeun (Julia) Cho, Ph.D.
Director
Division of Generic Drug Bioequivalence Evaluation
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: Review of surveillance inspection of (b) (4)
(b) (4) covering multiple
ANDAs/NDAs

Inspection summary

The Office of Study Integrity and Surveillance (OSIS) conducted a surveillance inspection of the analytical portion of the (b) (4) (ow) performed at (b) (4) between (b) (4) (b) (4). No significant deficiencies were observed and no Form FDA 483 was issued at the close of the inspection. Based on the inspection findings, we recommend accepting data

(b) (4)

from all studies conducted at (b) (4) in pending ANDAs/NDAs for further Agency (FDA) review.

Inspected studies

Please note that not all the studies listed in Appendix 1 were audited by the OSIS reviewers during the inspection. Therefore, OSIS's recommendation for all studies listed in Appendix 1 is based on the evaluation of the studies selected for the audit (see Table 1).

Table 1: List of pending ANDA/NDAs with study samples analyzed at (b) (4) audited during the current inspection

Application	Study Number*	Drug Product
NDA 209400	150075	Omeprazole delayed-release orally disintegrating 20 mg tablet

(b) (4)

The audit of the studies listed in Table 1 included a thorough examination of the facility, equipment, records for method validation and study sample analysis, SOPs, sample management/storage documentations, and instrument audit trails, as well as interviews and discussions with management and staff.

Recommendation

Based on the inspectional findings and overall evaluation of bioanalytical study conduct at (b) (4) the OSIS reviewers concluded that the data from the studies listed in Table 1 are reliable. Based on this conclusion, we recommend accepting the ANDAs/NDAs listed in Appendix 1 (which includes the studies in Table 1) for further Agency (FDA) review.

Final Classification:

NAI:

(b) (4)

(FEI:

(b) (4)

(b) (4)

CC:

OTS/OSIS/Kassim/Choe/Taylor/Haidar/Kadavil/Fenty-Stewart/Nkah
/Miller/Johnson

OTS/OSIS/DNDBE/Bonapace/Dasgupta/Biswas/Ayala/Yeh

OTS/OSIS/DGDBE/Cho/Murphy/Skelly/Choi/Au/Getie-Kehtie

OTS/OCP/DCPIII/Bashaw

OGD/OB/Conner

OND/ODEIV/DNDP/Salvatore/Michele

OND/ODEIII/DBRUP/Grayson/Joffe

Draft: MG 2/15/2017, 2/23/2017; LY 02/17/2017

Edit: SA 02/22/2017, 2/23/2017; JC 2/26/2017

ECMS: Cabinets/CDER_OC/OSI/Division of Bioequivalence & Good
Laboratory Practice Compliance/INSPECTIONS/BE Program/Analytical
Sites/ (b) (4)

OSI file #s:

(b) (4)

(b) (4)

FACTS:

(b) (4)

Appendix 1-Pending ANDA/NDAs with study samples analyzed at

(b) (4)

Application	Study #	Study Title	Dates of sample analysis	Audited by OSIS?
NDA 209400	150075	Randomized, Open-Label, 4-Way Crossover Bioequivalence Study of Omeprazole Delayed-Release Orally Disintegrating Tablet 20 mg and Omeprazole Delayed-Release Tablet (Reference) Following a 20 mg Dose in Healthy Subjects Under Fasting Conditions	1/4/16 to 1/15/16	Yes

(b) (4)

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

/s/

MELKAMU GETIE KEBTIE
03/09/2017

LI-HONG P YEH
03/09/2017

STANLEY AU
03/09/2017

SEONGEUN CHO
03/09/2017

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data)]

Application Information		
NDA # 209400	NDA Supplement #: S- N/A	Efficacy Supplement Category: ☐ New Indication (SE1) ☐ New Dosing Regimen (SE2) ☐ New Route Of Administration (SE3) ☐ Comparative Efficacy Claim (SE4) ☐ New Patient Population (SE5) ☐ Rx To OTC Switch (SE6) ☐ Accelerated Approval Confirmatory Study (SE7) ☐ Labeling Change With Clinical Data (SE8) ☐ Manufacturing Change With Clinical Data (SE9) ☐ Animal Rule Confirmatory Study (SE10)
Proprietary Name: TBD/Proprietary Name Review Request not submitted by Sponsor Established/Proper Name: omeprazole Dosage Form: delayed-release, orally disintegrating tablet Strengths: 20 mg		
Applicant: Dexcel Pharma Technologies, Ltd. Agent for Applicant (if applicable): CBR International Corp		
Date of Application: 09/06/16 Date of Receipt: 09/06/16 Date clock started after Unacceptable for Filing (UN): N/A		
PDUFA Goal Date: 07/06/17		Action Goal Date (if different): N/A
Filing Date: 11/05/16		Date of Filing Meeting: 10/25/16
Chemical Classification (original NDAs only) : ☐ Type 1- New Molecular Entity (NME); NME and New Combination ☐ Type 2- New Active Ingredient; New Active Ingredient and New Dosage Form; New Active Ingredient and New Combination ☐ Type 3- New Dosage Form; New Dosage Form and New Combination ☐ Type 4- New Combination ☒ Type 5- New Formulation or New Manufacturer ☐ Type 7- Drug Already Marketed without Approved NDA ☐ Type 8- Partial Rx to OTC Switch ☐ Type 9-New Indication or Claim (will <u>not</u> be marketed as a separate NDA after approval) ☐ Type 10-New Indication or Claim (will be marketed as a separate NDA after approval)		
Proposed indication(s)/Proposed change(s): Treatment of frequent heartburn (occurs 2 or more days a week) in adults age 18 years and older.		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:		☐ 505(b)(1) ☒ 505(b)(2) ☐ 505(b)(1) ☐ 505(b)(2)
<i>If 505(b)(2)NDA/NDA Supplement: Draft the “505(b)(2) Assessment” review found at:</i> http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499 .		

Type of BLA	☐ 351(a) ☐ 351(k)
If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team	
Review Classification: The application will be a priority review if: - A complete response to a pediatric Written Request (WR) was included (a partial response to a WR that is sufficient to change the labeling should also be a priority review – check with DPMH) - The product is a Qualified Infectious Disease Product (QIDP) - A Tropical Disease Priority Review Voucher was submitted - A Pediatric Rare Disease Priority Review Voucher was submitted	☒ Standard ☐ Priority ☐ Pediatric WR ☐ QIDP ☐ Tropical Disease Priority Review Voucher ☐ Pediatric Rare Disease Priority Review Voucher
Resubmission after withdrawal? ☐	Resubmission after refuse to file? ☐
Part 3 Combination Product? ☐ If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults	☐ Convenience kit/Co-package ☐ Pre-filled drug delivery device/system (syringe, patch, etc.) ☐ Pre-filled biologic delivery device/system (syringe, patch, etc.) ☐ Device coated/impregnated/combined with drug ☐ Device coated/impregnated/combined with biologic ☐ Separate products requiring cross-labeling ☐ Drug/Biologic ☐ Possible combination based on cross-labeling of separate products ☐ Other (drug/device/biological product)

☐ Fast Track Designation ☐ Breakthrough Therapy Designation <i>(set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)</i> ☐ Rolling Review ☐ Orphan Designation ☐ Rx-to-OTC switch, Full ☐ Rx-to-OTC switch, Partial ☒ Direct-to-OTC Other:	☐ PMC response ☐ PMR response: ☐ FDAAA [505(o)] ☐ PREA deferred pediatric studies (FDCA Section 505B) ☐ Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) ☐ Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)			
Collaborative Review Division (if OTC product): DGIEP				
List referenced IND Number(s): PIND 127169				
Goal Dates/Product Names/Classification Properties	YES	NO	NA	Comment
PDUFA/BsUFA and Action Goal dates correct in the electronic archive? If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.	☒	☐		
Are the established/proper and applicant names correct in electronic archive? If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name	☒	☐		

to the supporting IND(s) if not already entered into electronic archive.					
Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, orphan drug)? Check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at: http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm If no, ask the document room staff to make the appropriate entries.		☒	☐	☐	
Application Integrity Policy		YES	NO	NA	Comment
Is the application affected by the Application Integrity Policy (AIP)? Check the AIP list at: http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm If yes, explain in comment column.		☐	☒		
If affected by AIP , has OC been notified of the submission? If yes , date notified:		☐	☐		
User Fees		YES	NO	NA	Comment
Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?		☒	☐		
User Fee Status <i>If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period from receipt. Review stops. Contact the User Fee Staff. If appropriate, send UN letter.</i>		Payment for this application (check daily email from UserFeeAR@fda.hhs.gov): ☒ Paid ☐ Exempt (orphan, government) ☐ Waived (e.g., small business, public health) ☐ Not required			
<i>If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Contact the User Fee Staff. If appropriate, send UN letter.</i>		Payment of other user fees: ☒ Not in arrears ☐ In arrears			
User Fee Bundling Policy <i>Refer to the guidance for industry, Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees at:</i> http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf		Has the user fee bundling policy been appropriately applied? <i>If no, or you are not sure, consult the User Fee Staff.</i> ☒ Yes ☐ No			
505(b)(2) (NDAs/NDA Efficacy Supplements only)		YES	NO	NA	Comment
Is the application a 505(b)(2) NDA? (Check the 356h form,		☒	☐		

cover letter, and annotated labeling). If yes , answer the bulleted questions below:																					
• Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?		☐	☒																		
• Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? [see 21 CFR 314.54(b)(1)].		☐	☒																		
• Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug [see 21 CFR 314.54(b)(2)]?		☐	☒																		
If you answered yes to any of the above bulleted questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs for advice.																					
• Is there unexpired exclusivity on another listed drug product containing the same active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? Check the Electronic Orange Book at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm		☐	☒																		
If yes, please list below: <table border="1"> <thead> <tr> <th>Application No.</th> <th>Drug Name</th> <th>Exclusivity Code</th> <th>Exclusivity Expiration</th> </tr> </thead> <tbody> <tr><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td></tr> </tbody> </table>						Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration												
Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration																		
<i>If there is unexpired, 5-year exclusivity remaining on another listed drug product containing the same active moiety, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2). Unexpired orphan or 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.</i>																					
Exclusivity	YES	NO	NA	Comment																	
Does another product (same active moiety) have orphan exclusivity for the same indication? Check the Orphan Drug Designations and Approvals list at: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm	☐	☒																			
If another product has orphan exclusivity , is the product considered to be the same product according to the orphan drug definition of sameness [see 21 CFR 316.3(b)(13)]?	☐	☐	☒																		
If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy																					
NDA/NDA efficacy supplements only: Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity?	☐	☒	☐																		
If yes, # years requested:																					
Note: An applicant can receive exclusivity without requesting it;																					

<i>therefore, requesting exclusivity is not required.</i>				
NDAs only: Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use?	☐	☒	☐	
If yes , did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)?	☐	☐	☒	
If yes, contact the Orange Book Staff (CDER-Orange Book Staff).				
BLAs only: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act?	☐	☐	☒	
If yes, notify Marlene Schultz-DePalo, CDER Purple Book Manager				
Note: Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.				

Format and Content				
Do not check mixed submission if the only electronic component is the content of labeling (COL).	☐ All paper (except for COL) ☒ All electronic ☐ Mixed (paper/electronic) ☒ CTD ☐ Non-CTD ☐ Mixed (CTD/non-CTD)			
If mixed (paper/electronic) submission , which parts of the application are submitted in electronic format?				
Overall Format/Content	YES	NO	NA	Comment
If electronic submission , does it follow the eCTD guidance? ¹ If not , explain (e.g., waiver granted).	☒	☐	☐	
Index: Does the submission contain an accurate comprehensive index?	☒	☐		
Is the submission complete as required under 21 CFR 314.50 (NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including: ☒ legible	☒	☐		

¹ <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm333969.pdf>

☒ English (or translated into English) ☒ pagination ☒ navigable hyperlinks (electronic submissions only)				
If no , explain.				
BLAs only: Companion application received if a shared or divided manufacturing arrangement?	☐	☐	☐	
If yes , BLA #				
Forms and Certifications				
Electronic forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, paper forms and certifications with hand-written signatures must be included. Forms include: user fee cover sheet (3397/3792), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.				
Application Form	YES	NO	NA	Comment
Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)?	☒	☐		
<i>If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].</i>				
Are all establishments and their registration numbers listed on the form/attached to the form?	☒	☐	☐	
Patent Information (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	☒	☐	☐	
Financial Disclosure	YES	NO	NA	Comment
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)?	☒	☐		
<i>Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].</i>				
<i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i>				
Clinical Trials Database	YES	NO	NA	Comment
Is form FDA 3674 included with authorized signature?	☒	☐		
<i>If yes, ensure that the application is also coded with the supporting document category, "Form 3674."</i>				
<i>If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant</i>				

Debarment Certification	YES	NO	NA	Comment
Is a correctly worded Debarment Certification included with authorized signature? <i>Certification is not required for supplements if submitted in the original application; If foreign applicant, <u>both</u> the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].</i> <i>Note: Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e., “[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.” Applicant may not use wording such as, “To the best of my knowledge...”</i>	☒	☐	☐	
Field Copy Certification (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included? <i>Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)</i> <i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i>	☐	☐	☒	
Controlled Substance/Product with Abuse Potential	YES	NO	NA	Comment
<u>For NMEs:</u> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)? <i>If yes, date consult sent to the Controlled Substance Staff:</i> <u>For non-NMEs:</u> <i>Date of consult sent to Controlled Substance Staff :</i>	☐	☐	☒	
Pediatrics	YES	NO	NA	Comment
<u>PREA</u> Does the application trigger PREA? <i>If yes, notify PeRC@fda.hhs.gov to schedule required PeRC meeting²</i>	☒	☐		PeRC review scheduled on June 7, 2017

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027829.htm>

Note: NDAs/BLAs/efficacy supplements for new active ingredients (including new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.				
If the application triggers PREA , is there an agreed Initial Pediatric Study Plan (iPSP)?	☒	☐	☐	Full Waiver requested and agreed upon.
<i>If no, may be an RTF issue - contact DPMH for advice.</i>				
If required by the agreed iPSP , are the pediatric studies outlined in the agreed iPSP completed and included in the application?	☐	☐	☒	
<i>If no, may be an RTF issue - contact DPMH for advice.</i>				
BPCA:				
Is this submission a complete response to a pediatric Written Request?	☐	☒		
<i>If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required³)</i>				
Proprietary Name	YES	NO	NA	Comment
Is a proposed proprietary name submitted?	☐	☒	☐	
<i>If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."</i>				
REMS	YES	NO	NA	Comment
Is a REMS submitted?	☐	☐	☒	
<i>If yes, send consult to OSE/DRISK and notify OC/OSI/DSC/PMSB via the CDER OSI RMP mailbox</i>				
Prescription Labeling	☒ Not applicable			
Check all types of labeling submitted.	☐ Package Insert (Prescribing Information)(PI) ☐ Patient Package Insert (PPI) ☐ Instructions for Use (IFU) ☐ Medication Guide (MedGuide) ☐ Carton labeling ☐ Immediate container labels ☐ Diluent labeling ☐ Other (specify)			
	YES	NO	NA	Comment
Is Electronic Content of Labeling (COL) submitted in SPL format?	☐	☐		
<i>If no, request applicant to submit SPL before the filing date.</i>				
Is the PI submitted in Physician Labeling Rule (PLR)	☐	☐		

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027837.htm>

format? ⁴				
If PI not submitted in PLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.</i>	☐	☐	☒	
For applications submitted on or after June 30, 2015: Is the PI submitted in Pregnancy and Lactation Labeling Rule (PLLR) format? Has a review of the available pregnancy, lactation, and females and males of reproductive potential data (if applicable) been included?	☐ ☐	☐ ☐	☒ ☒	
For applications submitted on or after June 30, 2015: If PI not submitted in PLLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLLR format before the filing date.</i>	☐	☐	☒	
Has all labeling [(PI, patient labeling (PPI, MedGuide, IFU), carton and immediate container labeling)] been consulted to OPDP?	☐	☐	☒	
Has PI and patient labeling (PPI, MedGuide, IFU) been consulted to OSE/DRISK? (send WORD version if available)	☐	☐	☒	
Has all labeling [PI, patient labeling (PPI, MedGuide, IFU) carton and immediate container labeling, PI, PPI been consulted/sent to OSE/DMEPA and appropriate CMC review office in OPQ (OBP or ONDP)?	☐	☐	☒	
OTC Labeling	☐ Not Applicable			
Check all types of labeling submitted.	☒ Outer carton label ☒ Immediate container label ☒ Blister card ☒ Blister backing label ☒ Consumer Information Leaflet (CIL) ☒ Physician sample ☐ Consumer sample ☐ Other (specify)			
	YES	NO	NA	Comment
Is electronic content of labeling (COL) submitted?	☒	☐		

4

<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/LabelingDevelopmentTeam/ucm025576.htm>

<i>If no, request in 74-day letter.</i>				
Are annotated specifications submitted for all stock keeping units (SKUs)?	☒	☐	☐	
<i>If no, request in 74-day letter.</i>				
If representative labeling is submitted, are all represented SKUs defined?	☐	☐	☒	
<i>If no, request in 74-day letter.</i>				
All labeling/packaging sent to OSE/DMEPA?	☐	☒	☐	DMEPA review not necessary
Other Consults	YES	NO	NA	Comment
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team)	☐	☒	☐	
<i>If yes, specify consult(s) and date(s) sent:</i>				
Meeting Minutes/SPAs	YES	NO	NA	Comment
End-of Phase 2 meeting(s)? Date(s):	☐	☒		Pre-IND Type B mtg held Oct 6, 2015
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? Date(s): May 9, 2016	☒	☐		
Any Special Protocol Assessments (SPAs)? Date(s):	☐	X		

ATTACHMENT

MEMO OF FILING MEETING

DATE: October 25, 2016

BACKGROUND: Pre-IND Type B meeting held with sponsor on October 6, 2015.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Alina Salvatore	Y
	CPMS/TL:	Dan Brum	Y
Cross-Discipline Team Leader (CDTL)	Francis Becker		Y
Division Director/Deputy	Karen Mahoney		Y
Office Director/Deputy	Theresa Michele		N
Clinical	Reviewer:	Ryan Raffaelli	Y
	TL:	Francis Becker	Y
Social Scientist Review (<i>for OTC products</i>)	Reviewer:		
	TL:		
OTC Labeling Review (<i>for OTC products</i>)	Reviewer:	Mary Vienna	Y
	TL:	Kevin Lorick	Y
Clinical Microbiology (<i>for antimicrobial products</i>)	Reviewer:		
	TL:		
Clinical Pharmacology	Reviewer:	Sandhaya Apparaju	Y
	TL:	Sue Chih Lee	Y
• Genomics	Reviewer:		
• Pharmacometrics	Reviewer:		
Biostatistics	Reviewer:		
	TL:		

Nonclinical (Pharmacology/Toxicology)	Reviewer:	Charlie Donald Thompson	Y
	TL:	Jane Sohn	Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Product Quality (CMC) Review Team:	ATL:	Swapan De	Y
	RBPM:	Thao Vu	Y
• Drug Substance	Reviewer:	Friedrich Burnett	Y
• Drug Product	Reviewer:	Elise Luong	Y
• Process	Reviewer:	Krishnaiah Yellela	Y
• Microbiology	Reviewer:		
• Facility	Reviewer:	Carl Lee	Y
• Biopharmaceutics	Reviewer:	Hansong Chen	Y
• Immunogenicity	Reviewer:		
• Labeling (BLAs only)	Reviewer:		
• Other (e.g., Branch Chiefs, EA Reviewer)	Danae Christodoulou		N
OMP/OMPI/DMPP (MedGuide, PPI, IFU)	Reviewer:		
	TL:		
OMP/OPDP (PI, PPI, MedGuide, IFU, carton and immediate container labeling)	Reviewer:		
	TL:		
OSE/DMEPA (proprietary name, carton/container labeling)	Reviewer:		
	TL:		
OSE/DRISK (REMS)	Reviewer:		
	TL:		
OC/OSI/DSC/PMSB (REMS)	Reviewer:		
	TL:		

Bioresearch Monitoring (OSI)	Reviewer:		
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers/disciplines			
Discipline (DGEIP Clinical) *For additional lines, highlight this group of cells, copy, then paste: select "insert as new rows"	Reviewer:	Marjorie Dannis	N
	TL:	Anil Rajpal	N
Other attendees	Jagjit Grewal		Y
	Betsy Scroggs		Y
	*For additional lines, right click here and select "insert rows below"		

FILING MEETING DISCUSSION:

GENERAL 505(b)(2) filing issues: - Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? - Did the applicant provide a scientific "bridge" demonstrating the relationship between the proposed product and the referenced product(s)/published literature? Describe the scientific bridge (e.g., information to demonstrate sufficient similarity between the proposed product and the listed drug(s) such as BA/BE studies or to justify reliance on information described in published literature):		☐ Not Applicable ☐ YES ☒ NO ☒ YES ☐ NO The scientific bridge is established per two bioequivalence studies conducted by the applicant. Study 150075 demonstrated that the proposed omeprazole DR orally disintegrating tablet is bioequivalent to NDA 022032 omeprazole DR tablets which is also held by Dexcel. The applicant cross-referenced their Study AA24171 from NDA 022032 which demonstrated that their omeprazole DR tablet was bioequivalent to the listed
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	drug Prilosec OTC (NDA 021229).
Per reviewers, are all parts in English or English translation? If no, explain:	☒ YES ☐ NO
Electronic Submission comments List comments:	☐ Not Applicable ☒ No comments

CLINICAL Comments:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☒ Review issues for 74-day letter
Clinical study site(s) inspections(s) needed? If no, explain:	☒ YES ☐ NO
- Advisory Committee Meeting needed? Comments: <i>If no, for an NME NDA or original BLA, include the reason. For example:</i> <i>this drug/biologic is not the first in its class</i> <i>the clinical study design was acceptable</i> <i>the application did not raise significant safety or efficacy issues</i> <i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i>	☐ YES Date if known: ☒ NO ☐ To be determined Reason:
If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? Comments:	☒ Not Applicable ☐ YES ☐ NO
CONTROLLED SUBSTANCE STAFF Abuse Liability/Potential Comments:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CLINICAL MICROBIOLOGY Comments:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter

CLINICAL PHARMACOLOGY Comments:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
Clinical pharmacology study site(s) inspections(s) needed?	☐ YES ☒ NO
BIOSTATISTICS Comments:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
NONCLINICAL (PHARMACOLOGY/TOXICOLOGY) Comments:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
PRODUCT QUALITY (CMC) Comments:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☒ Review issues for 74-day letter
<u>New Molecular Entity (NDAs only)</u> Is the product an NME?	☐ YES ☒ NO
<u>Environmental Assessment</u> Categorical exclusion for environmental assessment (EA) requested? If no, was a complete EA submitted? Comments:	☒ YES ☐ NO ☐ YES ☐ NO
<u>Facility Inspection</u> Establishment(s) ready for inspection? Comments:	☐ Not Applicable ☒ YES ☐ NO

<u>Facility/Microbiology Review (BLAs only)</u> Comments:	☐ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
<u>CMC Labeling Review (BLAs only)</u> Comments:	☐ Review issues for 74-day letter
APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs) • Were there agreements made at the application's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application? • If so, were the late submission components all submitted within 30 days?	☐ N/A ☐ YES ☐ NO ☐ YES ☐ NO
• What late submission components, if any, arrived after 30 days?	
• Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?	☐ YES ☐ NO
• Is a comprehensive and readily located list of all clinical sites included or referenced in the application?	☐ YES ☐ NO
• Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?	☐ YES ☐ NO

REGULATORY PROJECT MANAGEMENT	
Signatory Authority: Karen Mahoney Date of Mid-Cycle Meeting (for NME NDAs/BLAs in “the Program” PDUFA V): 21st Century Review Milestones (see attached) (listing review milestones in this document is optional): Comments:	
REGULATORY CONCLUSIONS/DEFICIENCIES	
☐	The application is unsuitable for filing. Explain why:
☒	The application, on its face, appears to be suitable for filing. <u>Review Issues:</u> ☐ No review issues have been identified for the 74-day letter. ☒ Review issues have been identified for the 74-day letter. <u>Review Classification:</u> ☒ Standard Review ☐ Priority Review
ACTION ITEMS	
☒	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into the electronic archive (e.g., chemical classification, combination product classification, orphan drug).
☐	If RTF, notify everyone who already received a consult request, OSE PM, and RBPM
☐	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
☐	If priority review, notify applicant in writing by day 60 (see CST for choices)
☒	Send review issues/no review issues by day 74
☐	Conduct a PLR format labeling review and include labeling issues in the 74-day letter
☐	Update the PDUFA V DARRTS page (for applications in the Program)
☐	Other

Annual review of template by OND ADRAAs completed: April 2016

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

/s/

ALINA W SALVATORE
06/02/2017