

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**22-032**

**OTHER REVIEW(S)**



Office of Nonprescription Products  
Division of Nonprescription Regulation Development

| <b>Labeling Review</b>   |  |
|--|--|
| <b>NDA #:</b> 22-032   | <b>Sponsor:</b> Dexcel Pharma Technologies Limited           |
| <b>Drug Product:</b> Omeprazole delayed-release tablets 20 mg  | <b>Stock Keeping Units:</b> 14-tablets inner carton          |
| <b>Submission Dates:</b> October 5, 2007 and November 28, 2007 | <b>Review Dates:</b> November 19, 2007 and November 29, 2007 |
| <b>Type of Submission:</b> NDA                                 | <b>Reviewer:</b> Mary S. Robinson                            |

### **Background**

This Dexcel Pharma Technologies Limited submission responds to the FDA June 14, 2007 tentative approval letter. The revisions in the draft labels and labeling are for the 14 tablets inner carton label, and package insert for omeprazole delayed release tablets (see attached).

At the request of FDA, the sponsor submitted an additional supplement on November 28, 2007 containing updated labeling for the 14-, 28-, and 42-outer count cartons. This is a review of the labeling contained in these two submissions.

### **Reviewer Comments**

The following comments on the labeling changes and requests may be conveyed to the sponsor. The sponsor made the following changes to the labeling:

#### **I. Principal Display Panel**

- A. 14-tablets inner carton, 14-, 28-, and 42- tablets outer cartons
  - 1. The textbox that surrounds the phrase "Treats Frequent Heartburn" is removed from the label.
  - 2. The textbox that surrounds the words "acid reducer" is removed from the label.

*This change is acceptable*

#### **II. Carton Top**

- A. 14-tablets inner carton and 14-tablets outer cartons
  - 1. The country of manufacture is added.
  - 2. The product name and unit dosage is deleted.
- B. 28- and 42- tablets outer cartons
  - 1. The words "acid reducer" are added to the product name and unit dosage.
  - 2. The country of manufacture is added.
  - 3. The word "printed" is added to the tamper evident statement to read:
    - "Safety Feature – Do not use if the printed tablet blister unit is open or torn."

*This change is acceptable*

#### **III. Carton Side**

- A. 14-tablets inner carton
  - 1. The tamper-evident statement is moved from the top panel to a side panel and the word "printed" is added to the statement to read:
    - "Safety Feature – Do not use if the printed tablet blister unit is open or torn."
- B. 28-tablets outer carton
  - 1. The words "acid reducer" are added the product name and unit dosage (right side and left side).
- C. 42-tablets outer carton

- 1. Right side. The words "acid reducer" are added the product name and unit dosage (right side).
- 2. Left side. Under inactive ingredients, the drug name \_\_\_\_\_ is changed to hypromellose to be consistent with the current USP nomenclature.

b(4)

*This change is acceptable*

**IV. Carton Bottom**

**A. 14-tablets inner carton and 14-, 28-tablets outer cartons**

- 1. Under inactive ingredients, the drug name \_\_\_\_\_ is changed to hypromellose to be consistent with the current USP nomenclature.

b(4)

*This change is acceptable*

**B. Package Insert**

Following the last paragraph of the package insert, sponsor added the manufacturer name, address, country of manufacturer and code numbers.

*This is acceptable*

**Reviewer's Recommendations**

Inform the sponsor that this application can be approved.

---

Mary S. Robinson, M.S  
 Regulatory Review Chemist,  
 ONP/DNRD

---

Debbie Lumpkins  
 Team Leader,  
 ONP/DNRD

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

/s/

-----  
Mary Robinson  
12/3/2007 12:49:00 PM  
INTERDISCIPLINARY

Debbie Lumpkins  
12/3/2007 01:04:28 PM  
INTERDISCIPLINARY



Office of Nonprescription Products  
Division of Nonprescription Regulation Development

| <b>Labeling Review</b>  |  |
|---|--|
| <b>NDA #:</b> 22-032  | <b>Sponsor:</b> Dexcel Pharma Technologies Limited   |
| <b>Drug Product:</b> Omeprazole delayed-release tablets 20 mg | <b>Stock Keeping Units:</b> 14-tablets inner carton, 14-tablets outer carton, 28-tablets carton, 42-tablets carton |
| <b>Submission Dates:</b> April 16, 2007                       | <b>Review Date:</b> March 29, 2007   |
| <b>Type of Submission:</b> NDA                                | <b>Reviewer:</b> Mary S. Robinson  |

**Background**

This Dexcel Pharma Technologies Limited submission responds to the FDA Discipline Review Letter dated April 13, 2007. As per the FDA's letter request, the sponsor incorporated the suggested changes in the submitted draft labeling. The revisions in the draft labels and labeling are for the 14 tablets inner, 14 tablets outer, 28 tablets, and 42 tablets cartons and package insert for omeprazole delayed release tablets (see attached). This is a review of the labeling contained in this submission.

**Reviewer Comments and Recommendations**

The following comments and recommendations on the labeling changes and requests may be conveyed to the sponsor.

The sponsor has made the following changes to the labeling:

**A. Carton Back (14-tablets inner carton, 14-tablets outer carton, 28-tablets carton, 42-tablets carton)**

1. Under "Warnings" the "Do not use" paragraph is consolidated as follows:

"Do not use if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.

*This change is acceptable. (Note: this change was not made in the package insert.)*

2. Under "Warnings," subheading "Ask a doctor or pharmacist before use if you are taking," the following two warnings are added as the last two bullets:

- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

*This change is acceptable*

3. Under "Other information" delete the period after the first statement as follows:

- read the directions, warnings, and package insert before use

**B. Package Insert**

1 Under the heading "Warnings and When to ask Your Doctor", the following two warnings are added as the last two bullets under the subheading "Ask a doctor or pharmacist before use if you are taking"

- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

*This change is acceptable*

2. NOTE: Under "Warnings" the "Do not use" paragraph is not reformatted as on the cartons. See A.1., above.

*This is acceptable.*

**Reviewer's Recommendations**

Inform the sponsor that this application can be approved. However, the period should be deleted on the back of the 14-tablets inner carton, 14-tablets outer carton, 28-tablets carton, and 42-tablets carton under the paragraph "Other information", after the first statement for consistency as follows:

- read the directions, warnings, and package insert before use

---

Mary S. Robinson, M.S.  
Regulatory Review Chemist,  
ONP/DNRD

---

Helen Cothran,  
Team Leader,  
ONP/DNRD

10 Page(s) Withheld

       Trade Secret / Confidential (b4)

X Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)

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

/s/

-----  
Mary Robinson  
5/29/2007 02:57:36 PM  
INTERDISCIPLINARY

Helen Cothran  
5/29/2007 03:16:22 PM  
INTERDISCIPLINARY



**Office of Nonprescription Products**  
**Division of Nonprescription Regulation Development**

| <b>Labeling Review</b>  |  |
|---|--|
| <b>NDA #:</b> 22-032  | <b>Sponsor:</b> Dexcel Pharma Technologies Limited   |
| <b>Drug Product:</b> Omeprazole delayed-release tablets 20 mg | <b>Stock Keeping Units:</b> 14-tablets inner carton, 14-tablets outer carton, 28-tablets carton, 42-tablets carton |
| <b>Submission Dates:</b> December 18, 2006                    | <b>Review Date:</b> March 29, 2007   |
| <b>Type of Submission:</b> NDA                                | <b>Reviewer:</b> Mary S. Robinson  |

**Background**

Dexcel Pharma Technologies Limited submits a labeling amendment dated December 18, 2006 referencing FDA's approvable letter of December 8, 2006. The amendment provides for revisions in the draft labels and labeling for the blister card, 14 tablets inner, 14 tablets outer, 28 tablets, and 42 tablets cartons and package insert for omeprazole delayed release tablets (see attached). In addition, the sponsor acknowledges that new drug interaction warnings are added to the prescription omeprazole products and are also being considered for labeling of the omeprazole-containing nonprescription drug products. This is a review of the labeling contained in this submission.

**Reviewer Comments**

The following comments and recommendations on the labeling changes and requests may be conveyed to the sponsor.

The sponsor has made the following changes to the labeling:

**A. Principal Display Panel**

\_\_\_\_\_

b(4)

*This change is acceptable.*

\_\_\_\_\_

b(4)

*This change is acceptable*

**B. Carton Back**

\_\_\_\_\_

b(4)

*This change is acceptable*

**C. Package Insert**

\_\_\_\_\_

b(4)

*This change is acceptable*

**Reviewer's Recommendations**

Inform the sponsor that the following changes must be made before this application can be approved:

1. Cartons (14 inner, 14 outer, 28 and 42 tablets).

a. Under "Warnings", subheading Allergy Alert, make the capital "O" in omeprazole a small "o".

b. Under "Warnings," subheading "Ask a doctor or pharmacist before use if you are taking," add as the last two bullets, the following two warnings:

- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

c. Under "Other information" place a bullet by the first statement in accordance with § 201.66(d)(4) and insert commas as follows:

- read the directions, warnings, and package insert before use.

2. Package insert

a. Under the heading "Warnings and When to ask Your Doctor" add, as the last two bullets, the following two warnings under the subheading "Ask a doctor or pharmacist before use if you are taking"

- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

3. If additional carton space is needed to make the changes described above, the sponsor may:

a. Consolidate the "Do not use" paragraph under "Warnings" as follows:

"Do not use if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.

b. Place one or more bulleted statements on a horizontal line in accordance with 201.66(d)(4),.

---

Mary S. Robinson, M.S.  
Regulatory Review Chemist,  
ONP/DNRD

---

Helen Cothran,  
Team Leader,  
ONP/DNRD

12 Page(s) Withheld

       Trade Secret / Confidential (b4)

X Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)

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

/s/

-----  
Mary Robinson  
4/9/2007 06:29:03 PM  
INTERDISCIPLINARY

Helen Cothran  
4/10/2007 11:23:33 AM  
INTERDISCIPLINARY



**Office of Nonprescription Products  
Labeling Review**

|   |  |
|---|--|
| <b>NDA #:</b> 22-032  | <b>Sponsor:</b> Dexcel Pharma Technologies Limited |
| <b>Drug Product:</b> Omeprazole delayed-release tablets 20 mg | <b># of Stock Keeping Units in Submission:</b> 4   |
| <b>Submission Dates:</b> August 25, 2006                      | <b>Review Date:</b> October 2, 2006                |
| <b>Type of Submission:</b> NDA                                | <b>Reviewer:</b> Mary S. Robinson                  |

**Background**

Dexcel Pharma Technologies Limited submits draft and annotated printed labeling for the blister card, 14 tablets, 28 tablets, and 42 tablets cartons and package insert for omeprazole delayed release tablets. This submission responds to questions raised by the FDA in a teleconference on August 1, 2006. The sponsor has also included a report from \_\_\_\_\_, entitled, "Evaluation of the Seven Count Blister Card, Peel-Push Style- F=4 for Child Resistant Effectiveness for Dexcel Pharma Technologies LTD." This is a review of the proposed labeling contained in this submission.

b(4)

**Stock Keeping Unit:** (describe unit) 14-tablet carton (not for resale; to be used in the 28 and 42 cartons), 14-tablet carton, 28-tablet carton, 42-tablet carton

**Information Included in the submission follows:**

| <b>Content of Submission</b>  | <b>Yes</b> | <b>No</b> |
|---|------------|-----------|
| A cover letter stating that the submission includes new labeling in the Drug Facts format for the drug product and shelf keeping unit(s);                           | ✓          |           |
| A table of contents or index  | ✓          |           |
| A representation of the proposed labeling, including any outserts, panel extensions, or other graphical or package techniques intended to be used with the product. | ✓          |           |

The information provided is adequate for review: Yes

**Reviewer Comments**

The following comments and recommendations on the labeling may be conveyed to the sponsor (see attachments).

**1. Carton Labeling**

\_\_\_\_\_ The final name of the proposed product is "Omeprazole Delayed Release Tablets 20 mg".

b(4)

This is acceptable.

**2. Blister Card**

Dexcel submitted signed certification that the proposed seven count blister card packaging for omeprazole delayed release tablets, 20 mg, is in compliance with 16 CFR 1700- Poison Prevention Packaging.

This is acceptable.

**3. Principal Display Panel**

a. On the 28 count carton front panel lower right, change the statement "One 14-day course of treatment" to read: "Two 14-day courses of treatment."

b. On the 42 count carton front panel lower right, change the statement "One 14-day course of treatment" to read: "Three 14-day courses of treatment".

b(4)

to

b(4)

**4. Carton Back**

Under the heading "Questions?" add the information to be inserted in this section.

**5. Package Insert**

a. Under the paragraph heading, "How to Take Omeprazole Delayed Release Tablets 20 mg," add periods after the 4<sup>th</sup> and 6<sup>th</sup> bulleted statements.

b. The paragraph heading "How is Omeprazole Delayed Release Tablets 20 mg Sold" needs to be changed to read: "How are Omeprazole Delayed Release Tablets 20 mg Sold".

**Reviewer's Recommendation**

Inform the sponsor that the changes stated above under 3 --**Principal Display Panel**, 4 -- **Carton Back**, and 5 --**Package Insert** for Omeprazole Delayed Release Tablets 20 mg need to be addressed and the labeling submitted to the agency for review before this application can be approved.

---

Mary S. Robinson, M.S.  
Regulatory Review Chemist,  
ONP/DNRD

---

Helen Cothran,  
Team Leader,  
ONP/DNRD

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

/s/

-----  
Mary Robinson  
11/17/2006 03:30:43 PM  
INTERDISCIPLINARY

Helen Cothran  
11/17/2006 04:07:12 PM  
INTERDISCIPLINARY