CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 20-520/S-015

Name: Zantac 75 Tablets

Sponsor: Pfizer Consumer Healthcare

Approval Date: February 28, 2005

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-520/S-015

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APPLICATION NUMBER:

NDA 20-520/S-015

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-520/S-015

Pfizer Consumer Healthcare
Attn: Dawn Parkin
Senior Manager, Regulatory Affairs
201 Tabor Road
Morris Plains, NJ 07950

Dear Ms. Parkin:

Please refer to your supplemental new drug application dated August 30, 2004, received August 31, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zantac 75 (75mg ranitidine) Tablets.

We acknowledge receipt of your submissions dated February 16 and February 24, 2005.

This supplemental new drug application provides revised labeling incorporating additional warning language.

We have completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling (for all package inserts, bottle labels, 1-count pouch, blister carton labels, and bottle carton labels submitted February 24, 2005), and must be formatted in accordance with the requirements of 21 CFR 201.66.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA.* Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved supplement NDA 20-520/S-015**." Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call LCDR Keith Olin, Regulatory Project Manager, at (301) 827-2293.

Sincerely,

{See appended electronic signature page}

Curtis Rosebraugh, M.D., M.P.H.
Deputy Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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

/s/

Curtis Rosebraugh
2/28/05 01:22:07 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-520/S-015

LABELING

Revised Labeling Text – Bottle Label

Zantac 75 (Ranitidine 75 mg Tablets)

IMPORTANT: Read the directions, consumer information leaflet and warnings before use. Keep the carton. It contains important information.

Active ingredient (in each tablet) Ranitidine 75 mg (as ranitidine hydrochloride 84 mg) ***Purpose*** Acid reducer ***Uses*** • relieves heartburn associated with acid indigestion and sour stomach • prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain foods and beverages ***Warnings*** **Allergy alert:** Do not use if you are allergic to ranitidine or other acid reducers. **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. • with other acid reducers. ***Ask a doctor before use if you have*** • frequent wheezing, particularly with heartburn • frequent **chest pain** • stomach pain • unexplained weight loss • nausea or vomiting • had heartburn over 3 months. This may be a sign of a more serious condition. • 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. **Stop use and ask a doctor if** • your heartburn continues or worsens • you need to take this product for more than 14 days. **If pregnant or breast-feeding,** ask a health professional before use. **Keep out of reach of children.** In case of overdose, get medical help or contact a Poison Control Center right away. ***Directions*** • adults and children 12 years and over: • to **relieve** symptoms, swallow 1 tablet with a glass of water • to **prevent** symptoms, swallow 1 tablet with a glass of water **30 to 60 minutes before** eating food or drinking beverages that cause heartburn • can be used up to twice daily (do not take more than 2 tablets in 24 hours) • children under 12 years: ask a doctor ***Other information*** • store at 20°-25°C (68°- 77° F) • avoid excessive heat or humidity • this product is sugar free

Dist:
PFIZER CONSUMER HEALTHCARE
Morris Plains, NJ 07950 USA
www.prodhelp.com

Bottle sealed with printed foil under cap. Do not use if foil is open or torn.

LOT:

EXP:

Please note:
Headings will be in contrasting color distinct from other text.

Revised Labeling Text – Bottle Carton

Zantac 75 (Ranitidine 75 mg Tablets)

Drug Facts

Active ingredient (in each tablet) ***Purpose***
Ranitidine 75 mg (as ranitidine hydrochloride 84 mg)..... Acid reducer

Uses

- relieves heartburn associated with acid indigestion and sour stomach
- prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain foods and beverages

Warnings

Allergy alert: Do not use if you are allergic to ranitidine or other acid reducers

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.
- with other acid reducers

Ask a doctor before use if you have

- frequent wheezing, particularly with heartburn
- frequent **chest pain**
- stomach pain
- unexplained weight loss
- nausea or vomiting
- had heartburn over 3 months. This may be a sign of a more serious condition.
- 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

Stop use and ask a doctor if

- your heartburn continues or worsens
- you need to take this product for more than 14 days

If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions

- adults and children 12 years and over:
  - to **relieve** symptoms, swallow 1 tablet with a glass of water
  - to **prevent** symptoms, swallow 1 tablet with a glass of water **30 to 60 minutes before** eating food or drinking beverages that cause heartburn
  - can be used up to twice daily (do not take more than 2 tablets in 24 hours)
- children under 12 years: ask a doctor

Other information

- do not use if printed foil under bottle cap is open or torn
- store at 20°-25°C (68°-77°F)
- avoid excessive heat or humidity
- this product is sugar free

Inactive ingredients hypromellose, magnesium stearate, microcrystalline cellulose, synthetic red iron oxide, titanium dioxide, triacetin

Questions? call **1-800-223-0182,** weekdays, 9 AM – 5 PM EST

Name and Place of Distributor

Dist: **PFIZER CONSUMER HEALTHCARE,** Morris Plains, NJ 07950 USA
www.prodhelp.com

Expiration Date:

mm/yyyy

Net Quantity

XX Tablets (XX Doses)

LOT:

EXP:

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-520/S-015

LABELING REVIEWS

Division of OTC Drug Products Labeling Review

NDA 20-520/SLR-015

Submission Date:	8/30/04
Received Date:	8/31/04
Drug product:	Zantac 75® Tablets
Active ingredient:	Ranitidine hydrochloride
Pharmacological category:	Acid reducer
Sponsor/Contact:	John Jacobs, VP Global Regulatory Affairs Pfizer Consumer Healthcare 201 Tabor Road Morris Plains, NJ 07950 (973)385-5532
Labeling submitted:	draft labeling text (and representative labeling) for: bottle carton (60-ct) bottle labels (60-ct) blister carton (4-ct) blister backing (4-ct) 1-tab pouch package insert
Reviewer:	Reynold Tan
Review date:	10/7/04
Project manager:	Keith Olin

Background: The sponsor submitted a prior approval labeling supplement for Zantac 75 Tablets in response to FDA's request letter, dated 11/5/03, which requests new class labeling for all OTC acid reducers (H_2 receptor antagonists and proton pump inhibitors). This class labeling requires new warning language in the Drug Facts labeling, based upon recommendations made at the 6/21/02 Nonprescription Drugs and Gastrointestinal Drugs Joint Advisory Committee meeting.

Reviewer's comments:

1.) *Comment:* For carton labels, bottle labels, and the 1-tab pouch label, under the **"Uses"** heading, the sponsor should insert the words "eating or drinking" in the prevention claim such that the claim reads: "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain foods and beverages."

2.) For carton labels, bottle labels, the 1-tab pouch label, and the package insert, the sponsor includes the newly required class warning language under the **"Do not use"** subheading but removes the warning "**Do not use** with other acid reducers".

Comment: The sponsor should include the "**Do not use** with other acid reducers" warning under the "**Do not use**" subheading 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.
- with other acid reducers

3.) Under the **"Ask a doctor before use if you have"** subheading, multiple bulleted statements appear on the same line (the fourth line of text for the 60-ct carton label, and the fourth and fifth lines for the 4-ct carton label). The additional bulleted statements appearing on the same line are not vertically aligned with bulleted statements on the previous line as required under 21 CFR 201.66(d)(4).

Comment: For carton labels, under the **"Ask a doctor before use if you have"** subheading, the sponsor must vertically align additional bulleted statements that appear on the same line of text with bulleted statements that appear on the previous line, as required under 21 CFR 201.66(d)(4).

4.) Under the **"Directions"** heading, the statement "can be used up to twice daily (up to 2 tablets in 24 hours)" is revised to "can be used up to twice daily (do not take more than 2 tablets in 24 hours)".

Comment: This change is acceptable.

5.) A "See Revised Warnings" flag appears on bottle and carton labels. The sponsor states that this flag is intended to remain on labels for six months.

Comment: This change is acceptable.

6.) The sponsor removed the four bar graphs from the package insert that show results from clinical studies for the relief/prevention of heartburn.

Comment: The removal of efficacy bar graphs was allowed for all of the Pepcid AC acid reducer products (NDA 20-325/SLR-017, 20-801/SLR-010, 20-902/SLR-007, and 20-958/SLR-010). Therefore, removal of the bar graphs is acceptable for Zantac 75.

Reviewer's recommendations:
The following comments can be conveyed to the sponsor:

1.) Under the **"Uses"** heading for carton labels, bottle labels, and the 1-tab pouch label, add the words "eating or drinking" to the prevention claim such that the claim reads: "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain foods and beverages".

2.) For carton labels, bottle labels, the 1-tab pouch label, and the package insert, include the "**Do not use** with other acid reducers" warning under the "**Do not use**" subheading 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.
- with other acid reducers

3.) For carton labels, under the **"Ask a doctor before use if you have"** subheading, additional bulleted statements that appear on the same line of text (fourth line of the 60-ct carton label, and fourth and fifth line of the 4-ct carton label) must be vertically aligned with bulleted statements that appear on the previous line, as required under 21 CFR 201.66(d)(4).

These recommended revisions must be made before this supplement can be approved.

Reynold Tan, Ph.D.
IDS/Biologist, HFD-560

Helen Cothran, B.S.
Team Leader, HFD-560

5 pages of draft labeling have been removed from this portion of the document.

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

/s/

Reynold Tan
10/8/04 04:08:31 PM
INTERDISCIPLINARY

Helen Cothran
10/8/04 04:54:05 PM
INTERDISCIPLINARY

Division of OTC Drug Products Labeling Review

NDA 20-520/SLR-015	Sponsor's FAX of 12/2/04
Submission Date:	12/2/04
Received Date:	12/2/04
Drug product:	Zantac 75® Tablets
Active ingredient:	Ranitidine hydrochloride
Pharmacological category:	Acid reducer
Sponsor/Contact:	Dawn Parkin, Regulatory Affairs Pfizer Consumer Healthcare 201 Tabor Road Morris Plains, NJ 07950 (973)385-4039
Labeling submitted:	carton label for AXID AR Tablets, 50-ct carton label for Prilosec OTC Tablets, 14-ct
Reviewer:	Reynold Tan
Review date:	1/14/05
Project manager:	Keith Olin

Background

The sponsor submitted labeling for Zantac 75 Tablets incorporating new class labeling for all OTC acid reducers (H_2 receptor antagonists and proton pump inhibitors) in a prior approval labeling supplement NDA 20-520/SLR-015 (8/30/04). FDA responded by recommending the following labeling changes to the submitted labeling (FDA FAX on 11/19/04):

- add the words "eating or drinking" to the prevention claim under the **"Uses"** heading to read "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain foods and beverages"
- include the "**Do not use** with other acid reducers" warning under the "**Do not use**" subheading
- vertically align bulleted statements as required under 21 CFR 201.66(d)(4) under the **"Ask a doctor before use if you have"** subheading

This review is in response to the sponsor's FAX on 12/2/04, which addresses these recommended labeling changes.

Reviewer's comments

1.) The sponsor requests the option of using '———" instead of "eating or drinking" for the prevention claim under the **"Uses"** heading because of space limitations on several package sizes. The sponsor states that the words ——— brought on by ——— food and beverages" is used in the ——— prevention claim.

Comment: The currently approved prevention claim for ——— reads "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain food and beverages" ——— FDA recommends that the prevention claim use this exact language for consistency in labeling for this product class.

2.) The sponsor includes the "**Do not use** with other acid reducers" warning under the "**Do not use**" subheading 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.
- with other acid reducers

Comment: Although the sponsor agreed to include the statement "**Do not use** with other acid reducers", the statement appears as "with other reducers", omitting the word "acid". The statement should include the word "acid".

3.) The sponsor proposes to align the second bullet on the fifth line ("■ stomach pain") with the second bullet on the fourth line ("■ frequent wheezing, particularly with heartburn") under the **"Ask a doctor before use if you have"** subheading for the 4-ct carton label. The sponsor states that the bulleting for Zantac 75 is similar to the bulleting on the approved Prilosec OTC carton label (appearing on the FDA website).

Comment: The sponsor's proposed alignment of the bullets does not correct the problem. Additional bulleted statements appearing on the same line must be vertically aligned with bulleted statements on the previous line, as required under 21 CFR 201.66(d)(4). This regulation requires that a line with multiple bulleted statements be preceded by a line with the same or a greater number of bulleted statements, with vertical alignment of the bullets. Therefore, the **"Ask a doctor before use if you have"** sections for the 4-ct and 60-ct carton labels do not conform to regulations. We note that the Prilosec OTC label does not conform to these bulleting regulations. The sponsor may reorder the bulleted statements in this section to address space limitations while conforming to regulations as follows:

Ask a doctor before use if you have
- ■frequent wheezing, particularly with heartburn
- ■frequent **chest pain**
- ■stomach pain
- ■unexplained weight loss
- ■nausea or vomiting
- ■had heartburn over 3 months. This may be a sign of a more serious condition.
- ■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

Reviewer's recommendations

The following comments can be conveyed to the sponsor:

1.) The currently approved prevention claim for ——— uses the words "eating or drinking" instead of "———". Therefore, under the **"Uses"** heading for carton labels, bottle labels, and the 1-tab pouch label, add the words "eating or drinking" to the prevention claim such that the claim reads: "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain food and beverages".

2.) For carton labels, bottle labels, the 1-tab pouch label, and the package insert, verify that the word "acid" appears in the statement "**Do not use** with other acid reducers" 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.
- with other acid reducers

3.) Align the bulleted statements under the **"Ask a doctor before use if you have"** section to conform to 21 CFR 201.66(d)(4). The sponsor's proposed alignment of the bullets does not correct the problem. The sponsor may reorder the bulleted statements in this section to address space limitations while conforming to regulations as follows:

Ask a doctor before use if you have
■frequent wheezing, particularly with heartburn ■frequent **chest pain** ■stomach pain
■unexplained weight loss ■nausea or vomiting
■had heartburn over 3 months. This may be a sign of a more serious condition.
■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

Additional bulleted statements appearing on the same line must be vertically aligned with bulleted statements on the previous line, as required under 21 CFR 201.66(d)(4). This regulation requires that a line with multiple bulleted statements be preceded by a line with the same or a greater number of bulleted statements, with vertical alignment of the bullets. Therefore, the sponsor's proposed **"Ask a doctor before use if you have"** sections for the 4-ct and 60-ct carton labels do not conform to regulations. We note that the Prilosec OTC label does not conform to these bulleting regulations.

These recommended revisions must be made before this supplement can be approved.

Reynold Tan, Ph.D.
IDS/Biologist, HFD-560

Helen Cothran, B.S.
Team Leader, HFD-560

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/s/

Reynold Tan
1/24/05 10:15:09 AM
INTERDISCIPLINARY

Helen Cothran
1/25/05 09:57:25 AM
INTERDISCIPLINARY

Division of OTC Drug Products Labeling Review

NDA 20-520/SLR-015	Sponsor's FAX of 2/24/05
Submission Date:	2/24/05
Received Date:	2/24/05
Drug product:	Zantac 75® Tablets
Active ingredient:	Ranitidine hydrochloride
Pharmacological category:	Acid reducer
Sponsor/Contact:	Dawn Parkin, Regulatory Affairs Pfizer Consumer Healthcare 201 Tabor Road Morris Plains, NJ 07950 (973)385-4039
Labeling submitted:	mock-up versions of 60-ct bottle carton label and bottle label
Reviewer:	Reynold Tan
Review date:	2/28/05
Project manager:	Keith Olin

Background

The sponsor submitted mock-up versions of a Zantac 75 bottle carton and bottle label, marked to signify intended changes. The sponsor stated that these changes will apply to all current count sizes for bottle carton, bottle label, blister carton, 1-ct pouch, and package insert.

FDA had suggested these changes upon review of labeling submitted under the labeling supplement NDA 20-520/SLR-015 (8/30/04), which incorporated new class labeling for all OTC acid reducers (H_2 receptor antagonists and proton pump inhibitors). FDA recommended labeling changes (FAX on 11/19/04) to which the sponsor responded (FAX on 12/2/04). In response to the sponsor's FAX on 12/2/04, FDA made these further comments:

1. Substituting the word "———" for "eating or drinking" in the prevention claim under **"Uses"** is not acceptable. The currently approved prevention claim for acid reducers reads "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain food and beverages".

2. The sponsor inadvertently omitted the word "acid" from the statement "**Do not use** with other acid reducers". The word "acid" must be included in the statement.

3. Bulleted statements under the **"Ask a doctor before use if you have"** section for the 4-ct and 60-ct carton labels do not conform to regulations, as required under 21 CFR 201.66(d)(4). This regulation requires that a line with multiple bulleted statements be preceded by a line with the same or a greater number of bulleted statements, with vertical alignment of the bullets.

Reviewer's comments

The sponsor stated their intention (FAX on 2/24/05) to make the following changes:

1) The prevention claim under the **"Uses"** heading is revised to read "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain food and beverages".

Comment: This change is acceptable.

2) The **"Do not use"** section is revised to read:

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.
¦ with other acid reducers

Comment: This change is acceptable.

3) The **"Ask a doctor before use if you have"** section is revised to conform with 21 CFR 201.66(d)(4).

Comment: The appearance and alignment of bulleted statements is acceptable.

Reviewer's recommendations

The following comments can be conveyed to the sponsor:

The labeling changes made to submitted (FAX 2/24/05) mock-up versions of the 60-ct Zantac 75 bottle carton and bottle label are acceptable. The sponsor stated that these labeling changes will apply to all current count sizes for bottle label, bottle carton, blister carton, 1-ct pouch, and package insert.

Reynold Tan, Ph.D.
IDS/Biologist, HFD-560

Helen Cothran, B.S.
Team Leader, HFD-560

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/s/

Reynold Tan
2/28/05 10:50:51 AM
INTERDISCIPLINARY

Helen Cothran
2/28/05 12:33:31 PM
INTERDISCIPLINARY

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-520/S-015

CORRESPONDENCE

Pfizer Consumer Healthcare
Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000

Consumer Healthcare Regulatory Affairs

August 30, 2004

Charles Ganley, M.D., Director
Division of Over the Counter Drug Products
Center for Drug Evaluation and Research
HFD-560, Room S205
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850

Mail to:
Central Document Room
Center for Drug Evaluation & Research
Food And Drug Administration
5901-B Ammendale Rd.
Beltsville, MD 20705

RE: **NDA 20-520; Zantac® 75 (ranitidine hydrochloride) Tablets 75 mg**
SUBJECT: **Prior Approval Supplement for nonprescription acid reducer class warning draft labeling**

Dear Dr Ganley:

Reference is made to Zantac 75® (ranitidine 75 mg [as ranitidine hydrochloride 84 mg]) 75 mg Tablets for Over-the-Counter Use approved December 19, 1995 and the most recent Annual Report submitted on August 3, 2004 for the period December 20, 2002 – December 19, 2003. Reference is made to the November 5, 2003 FDA correspondence for NDA 20-520, for Zantac 75 (ranitidine hydrochloride) Tablets, requesting class warning language in response to the discussions at the June 21, 2002, joint meeting of the Nonprescription Drugs Advisory Committee and the Gastrointestinal Drugs Advisory Committee for Prilosec for OTC use. We are submitting a Prior Approval Supplement which includes draft labeling with these class warnings incorporated.

The labeling for this prior approval supplement is being submitted electronically. In accordance with the Guidance for Industry, Providing Regulatory Submissions in Electronic Format, General Considerations, one CD-ROM is included in both the Review and Archive copies of this Supplement. The two CD-ROMs were scanned with McAffee Virus Scan, Version 4.5.1 SP1, Virus Definitions 4.0.4381, Scan Engine 4.3.20 and are virus free.

The contents of this submission are identified in the appended Table of Contents. Draft labeling, including draft labeling text, is included in PDF format in the PDF Electronic Components CD-ROM. Also enclosed is a second CD-ROM containing the draft labeling text in MS Word format as review aid for editing purposes.

This submission contains confidential/trade secret information to which all claims of privilege and confidentiality are asserted in both statutory and common law. Further dissemination may only be made with the express written permission of Pfizer Consumer Healthcare.

Please do not hesitate to contact me directly at 973-385-4039 should you have any questions or comments concerning this Prior Approval Supplement.

Sincerely,

Dawn Parkin

Dawn Parkin
Senior Manager, Regulatory Affairs

cc: Keith Olin, HFD-560 (Desk Copy)

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-520/S-015

PRIOR APPROVAL SUPPLEMENT

Pfizer Consumer Healthcare
Attention: Dawn Parker
Senior Manager, Regulatory Affairs
201 Tabor Road
Morris Plain, NJ 07950

Dear Ms. Parker:

We have received your supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Zantac 75 (75mg ranitidine) Tablets

NDA Number: 20-520

Supplement number: 015

Date of supplement: August 30, 2004

Date of receipt: August 31, 2004

This supplemental application provides revised labeling incorporating additional warning language.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on October 29, 2004, in accordance with 21 CFR 314.101(a). If the application is filed, the goal date will be February 28, 2005.

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Over-the-Counter Drug Products, HFD-560
Attention: Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Over-the-Counter Drug Products, HFD-560
9201 Corporate Blvd
Rockville, Maryland 20850

If you have any question, call LCDR Keith Olin, Regulatory Project Manager, at (301) 827-2293.

Sincerely,

{See appended electronic signature page}

David R. Hilfiker
Chief Management Staff
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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/s/

David Hilfiker
10/13/04 02:00:56 PM

Food and Drug Administration
Center for Drug Evaluation and Research
Division of OTC Drug Products
Office of Drug Evaluation V

FACSIMILE TRANSMITTAL SHEET

DATE: 11/17/04

To: Dawn Parkin	**From:** LCDR Keith J. Olin R.Ph. Regulatory Project Manager
Company: Pfizer Consumer Healthcare	Division of Over-the-Counter Drug Products
Fax number: 973-385-4300	**Fax number:** (301) 827-2315
Phone number: 973-385-4039	**Phone number:** (301) 827-2249

Subject: Zantac 75 Labeling Supplement Comments NDA 20-520/S-015

Total no. of pages including cover: 2

Comments: Please, review comments and respond as soon as possible

Document to be mailed: YES X NO

Please refer to your supplemental new drug application NDA 20-520/S-015 dated August 31, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zantac 75 (75mg ranitidine) Tablets.

We are providing preliminary comments related to the submitted labeling. In order to ensure a timely action for this new drug application, we request that you respond to the issues listed below as soon as possible. You can fax your response to LCDR Keith Olin at (301) 827-2315.

The following changes apply to the carton label, bottle label, and 1-tablet pouch label.

1.) Add the words "eating or drinking" to the prevention claim under the **"Uses"** heading for carton labels, bottle labels, and the 1-tablet pouch label, so that the claim reads: "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain foods and beverages".

2.) Include the "**Do not use** with other acid reducers" warning under the "**Do not use**" subheading for the carton labels, bottle labels, the 1-tablet pouch label, and the package insert, 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.
- with other acid reducers

The following changes apply to the carton label.

1.) Under the **"Ask a doctor before use if you have"** subheading, additional bulleted statements that appear on the same line of text (fourth line of the 60-count carton label, and fourth and fifth line of the 4-count carton label) must be vertically aligned with bulleted statements that appear on the previous line, as required under 21 CFR 201.66(d)(4).

If you have any questions, contact LCDR Keith Olin, Regulatory Project Manager, at 301-827-2293.

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

/s/

Keith Olin
11/23/04 04:02:39 PM
CSO

Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000

FAX TRANSMITTAL

To:	LCDR Keith J. Olin, R.Ph. Regulatory Project Manager
Company:	Food and Drug Administration Division of Over-the-Counter Drug Products
Fax Number:	(301) 827-2315
Telephone Number:	(301) 827-2249
From:	DP **Dawn Parkin, Regulatory Affairs**
Date:	December 2, 2004
No. of Pages (including cover):	5
Fax Number:	973-385-4300
Telephone Number:	973-385-4039
Subject:	**Response to Zantac 75 Labeling Supplement Comments NDA 20-520/S-015**

Mr. Olin,

Listed below are the comments from Pfizer Consumer Healthcare as related to the November 19, 2004 FDA facsimile comments for Zantac 75 Labeling Supplement NDA 20-520/S-015. We respond with the following:

Carton label, bottle label and 1-tablet pouch label comments

1. We request the option of using "———" instead of "eating or drinking" for the prevention claim under the **"Uses"** heading for carton labels, bottle labels and the 1-tablet pouch label so the claim reads: "prevents heartburn associated with acid indigestion and sour stomach brought on by ——— certain foods and beverages." This request is based on space limitations on several package sizes of Zantac 75 and "——— brought on by ——— food and beverages" is the current language on the ——— carton label. (See attached copy of carton label).

   ✓ "———" instead of "eating or drinking"

2. We are in agreement with the comment: Include the "Do not use with other acid reducers" warning under the **"Do not use"** subheading for the carton labels, bottle labels, the 1-tablet pouch label and package insert and will change to:

   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.
   - with other reducers

   ✓ OK

Carton label only comment

Under the **"Ask a doctor before use if you have"** subheading on the 4 count carton label we will vertically align the second bullet on the fifth line that states "• stomach pain" with the second bullet on the fourth line that states " • frequent wheezing, particularly with heartburn". For both the 4 count and 60 count carton label this type of bulleting does not appear to be inconsistent with regulations based on the June 20, 2003 FDA approved Rx-to OTC switch product Prilosec OTC carton label. The Prilosec OTC carton label has bulleting similar to Zantac 75. (See attached carton label from FDA website).

If you have any question, please contact Dawn Parkin, Senior Manager-Regulatory Affairs at (973) 385-4039.

APPEARS THIS WAY
ON ORIGINAL

Pfizer Consumer Healthcare
Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000

ORIGINAL

Consumer Healthcare Regulatory Affairs

SLR015(BL)
NDA SUPPL AMENDMENT

RECEIVED
FEB 17 2005
MEGA / CDER

February 16, 2005

Charles Ganley, M.D., Director
Division of Over the Counter Drug Products
Center for Drug Evaluation and Research
HFD-560, Room S205
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850

Mail to:
Central Document Room
Center for Drug Evaluation & Research
Food And Drug Administration
5901-B Ammendale Rd.
Beltsville, MD 20705

RE: **NDA 20-520; Zantac® 75 (ranitidine hydrochloride) Tablets 75 mg**
SUBJECT: **Response to November 19, 2004 FDA facsimile comments for Prior Approval Supplement for nonprescription acid reducer class warning draft labeling**

Dear Dr Ganley:

Reference is made to Zantac 75® (ranitidine 75 mg [as ranitidine hydrochloride 84 mg]) 75 mg Tablets for Over-the-Counter Use approved December 19, 1995 and the most recent Annual Report submitted on August 3, 2004 for the period December 20, 2002 – December 19, 2003. Reference is made to the November 5, 2003 FDA correspondence for NDA 20-520, for Zantac 75 (ranitidine hydrochloride) Tablets, requesting class warning language in response to the discussions at the June 21, 2002, joint meeting of the NonPrescription Drugs Advisory Committee and the Gastrointestinal Drugs Advisory Committee for Prilosec for OTC use. Reference is made to the November 19, 2004 FDA facsimile comments for Zantac 75 Labeling Supplement NDA 20-520/S-015. Pfizer Consumer Healthcare responded to these comments via facsimile on December 2, 2004. However, as per a phone conversation on January 28, 2005 with Mr. Keith Olin-FDA, a paper version also needs to be submitted. Listed below are the Pfizer Consumer Healthcare comments that were sent via facsimile on December 2, 2004 to Mr. Olin-FDA in response to the November 19, 2004 FDA facsimile:

Carton label, bottle and 1-tablet pouch label comments

1. We request the option of using "————" instead of "eating or drinking" for the prevention claim under the **"Uses"** heading for carton labels, bottle labels and the 1-tablet pouch label so the claim reads: "prevents heartburn associated with acid indigestion and sour stomach brought on by———— certain foods and beverages." This request is based on space limitations on several package sizes of Zantac 75 and '———— ———— brought on by———— food and beverages" is the current language on the ———— carton label. (See attached copy of carton label).

2. We are in agreement with the comment: Include the "**Do not use** with other acid reducers" warning under the "**Do not use**" subheading for the carton labels, bottle labels, the 1-tablet pouch label and package insert and will change to:

   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.
   - with other acid reducers

Carton label only comment

Under the "**Ask a doctor before use if you have**" subheading on the 4 count carton label we will vertically align the second bullet on the fifth line that states "• stomach pain" with the second bullet on the fourth line that states "• frequent wheezing, particularly with heartburn". For both the 4 count and 60 count carton label this type of bulleting does not appear to be inconsistent with regulations based on the June 20, 2003 FDA approved Rx-to-OTC switch product Prilosec OTC carton label. The Prilosec OTC carton label has bulleting similar to Zantac 75. (See attached carton label from FDA website).

This submission contains confidential/trade secret information to which all claims of privilege and confidentiality are asserted in both statutory and common law. Further dissemination may only be made with the express written permission of Pfizer Consumer Healthcare.

Please do not hesitate to contact me directly at 973-385-4039 should you have any questions or comments concerning this Amendment to Prior Approval Supplement #15.

Sincerely,

Dawn Parkin

Dawn Parkin
Senior Manager, Regulatory Affairs

Food and Drug Administration
Center for Drug Evaluation and Research
Division of OTC Drug Products
Office of Drug Evaluation V

FACSIMILE TRANSMITTAL SHEET

DATE:

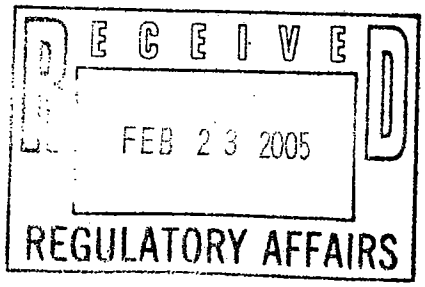
To: Dawn Parkin	**From:** LCDR Keith Olin, RPh. Regulatory Project Manager
Company: Pfizer	Division of Over-the-Counter Drug Products
Fax number: 973-385-4300	**Fax number:** (301) 827-2315
Phone number: 973-385-4039	**Phone number:** (301) 827-2293

Subject: Labeling Comments NDA 20-520/S-015

Total no. of pages including cover: 2

These are the discussion point per our conversation about the label on 2/15/2004.

Document to be mailed: ☐ YES ☑ NO



Please refer to your August 30, 2004 supplement new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zantac 75 (75mg ranitidine) Tablets.

We have reviewed the referenced material and have the following preliminary comments and recommendations related to the labeling:

1) Revise the heading under "**Uses**" for the carton, bottle, and 1-tab pouch labels, by adding the words "eating or drinking" to the prevention claim such that the claim reads "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain food and beverages".

2) Revise the heading under "**Do not use**" for the carton, bottle, 1-tab pouch labels, and package insert to add the word "acid" in the statement such that the claim reads "with other acid reducers".

3) Align the bulleted statements under the "**Ask a doctor before use if you have**" section to conform to 21 CFR 201.66(d)(4). Additional bulleted statements appearing on the same line must be vertically aligned with bulleted statements on the previous line. This regulation requires that a line with multiple bulleted statements be preceded by a line with the same or a greater number of bulleted statements, with vertical alignment of the bullets.

We are providing these comments to you to give you preliminary notice of issues that we have identified. These comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. In order to ensure a timely action for this new drug application, we request that you respond to the issues listed above by February 24, 2005.

If you have any questions, contact LCDR Keith Olin, Regulatory Project Manager, at (301) 827-2293.

Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000

FAX TRANSMITTAL

To:	LCDR Keith J. Olin, R.Ph.
	Regulatory Project Manager
Company:	Food and Drug Administration
	Division of Over-the-Counter Drug Products
Fax Number:	(301) 827-2315
Telephone Number:	(301) 827-2249
From:	**Dawn Parkin, Regulatory Affairs**
Date:	February 24, 2005
No. of Pages (including cover):	**4**
Fax Number:	973-385-4300
Telephone Number:	973-385-4039
Subject:	**Response to Zantac 75 Labeling Supplement Comments NDA 20-520/S-015**

Mr. Olin,

Attached is the mock-up versions of a Zantac 75 bottle carton and bottle label with the suggested FDA changes (listed below) as related to the February 22, 2005 FDA facsimile comments for Zantac 75 Labeling Supplement NDA 20-520/S-015. These labeling revisions will apply to all current count sizes for bottle label, bottle carton, blister carton, 1 count pouch and package insert.

1) Under the "**Uses**" heading the prevention claim has been revised to read: "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain food and beverages".
2) The "**Do not use**" section has been revised to read:

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.
- with other acid reducers

3) The "**Ask a doctor before use if you have**" section has been revised in order to conform with 21 CFR 201.66(d) (4) which is related to vertical alignment of bulleted statements. See below for this revision.

Ask a doctor before use if you have

- frequent wheezing, particularly with heartburn
- frequent **chest pain**
- stomach pain
- unexplained weight loss
- nausea or vomiting
- had heartburn over 3 months. This may be sign of a more serious condition.
- 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

An official copy of this facsimile will be submitted to the agency. If you have any questions, please contact Dawn Parkin, Senior Manager-Regulatory Affairs at (973) 385-4039.

APPEARS THIS WAY
ON ORIGINAL

Pfizer Consumer Healthcare
Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000

ORIGINAL

Consumer Healthcare Regulatory Affairs

February 28, 2005

Charles Ganley, M.D., Director
Division of Over the Counter Drug Products
Center for Drug Evaluation and Research
HFD-560, Room S205
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850

RE: **NDA 20-520 S-015; Amendment to Prior Approval**
Zantac® 75 (ranitidine hydrochloride) Tablets 75 mg
SUBJECT: **Response to February 22, 2005 FDA facsimile comments for Prior Approval Supplement for nonprescription acid reducer class warning draft labeling**

Dear Dr Ganley:

Reference is made to Zantac 75® (ranitidine 75 mg [as ranitidine hydrochloride 84 mg]) 75 mg Tablets for Over-the-Counter Use approved December 19, 1995 and the most recent Annual Report submitted on August 3, 2004 for the period December 20, 2002 – December 19, 2003. Reference is made to the November 5, 2003 FDA correspondence for NDA 20-520, for Zantac 75 (ranitidine hydrochloride) Tablets, requesting class warning language in response to the discussions at the June 21, 2002, joint meeting of the NonPrescription Drugs Advisory Committee and the Gastrointestinal Drugs Advisory Committee for Prilosec for OTC use. Reference is made to the November 19, 2004 FDA facsimile comments for Zantac 75 Labeling Supplement NDA 20-520/S-015. Pfizer Consumer Healthcare responded to these comments via facsimile on December 2, 2004 and on February 16, 2005 via a hard copy as an amendment to Supplement #15. Reference is made to the February 22, 2005 FDA facsimile. Listed below are the Pfizer Consumer Healthcare comments that were sent via facsimile on February 24, 2005 to Mr. Olin-FDA in response to the February 22, 2005 FDA facsimile:

Attached are the mocked-up labeling and labeling text versions of a Zantac 75 bottle carton and bottle label with the suggested FDA changes (listed below) as related to the February 22, 2005 FDA facsimile comments for Zantac 75 Labeling Supplement NDA 20-520/S-015. These labeling revisions are applicable to all current count sizes for bottle label, bottle carton and blister carton, 1-count pouch and package insert.

1. Under the **"Uses"** heading the prevention claim has been revised to read: "prevents heartburn associated with acid indigestion and sour stomach brought on by eating or

drinking certain foods and beverages".

2. The "**Do not use**" section has been revised to read::

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.
- with other acid reducers

3. The "**Ask a doctor before use if you have**" section has been revised in order to conform with 21 CFR 201.66(d)(4) which is related to vertical alignment of bulleted statements. See below for this revision:

Ask a doctor before use if you have
- frequent wheezing, particularly with heartburn
- frequent **chest pain**
- stomach pain
- unexplained weight loss
- nausea or vomiting
- had heartburn over 3 months. This may be a sign of a more serious condition.
- 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

This submission contains confidential/trade secret information to which all claims of privilege and confidentiality are asserted in both statutory and common law. Further dissemination may only be made with the express written permission of Pfizer Consumer Healthcare.

Please do not hesitate to contact me directly at 973-385-4039 should you have any questions or comments concerning this Amendment to Prior Approval Supplement #15.

Sincerely,

Dawn Parkin

Dawn Parkin
Senior Manager, Regulatory Affairs