

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-801/S-012

Trade Name: Pepcid AC 10mg and 20mg chewable tablet

Generic Name: famotidine

Sponsor: Merck & Co., Inc.

Approval Date: December 17, 2007

Purpose: A new 20mg strength formulation with three different flavors and new labels for Pepcid AC chewable tablet for the nonprescription treatment of frequent heartburn.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
20-801/S-012

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Other Action Letters	
Labeling	X
Summary Review	
Officer/Employee List	
Office Director Memo	
Cross Discipline Team Leader Review	
Medical Review(s)	X
Chemistry Review(s)	X
Environmental Assessment	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/Biopharmaceutics Review(s)	X
Other Reviews	X
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	
Administrative/Correspondence Document(s)	X

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-801/S-012

APPROVAL LETTER



NDA 20-801/S-012

Merck & Co., Inc.
Attention: Brenda McGuire, M.S., R.N.
Associate Director, Worldwide OTC Regulatory Affairs
Sumneytown Pike
P.O. Box 4, UN-D129
West Point, PA 19486

Dear Ms. McGuire:

Please refer to your supplemental new drug application dated March 23, 2007, received March 23, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pepcid AC (10mg famotidine) chewable tablet.

We acknowledge receipt of your submission dated July 5, 2007.

This supplemental new drug application provides for a new 20 mg strength formulation with three different flavors and new labels for Pepcid AC chewable tablet for the nonprescription treatment of frequent heartburn. Per your March 23, 2007 submission, this new formulation and strength will replace the old formulation and the currently marketed 10 mg strength chewable tablet will be discontinued.

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:

- 1) Pepcid AC Chewable (20 mg famotidine) tablet
 - a) Carton labels with Drug Facts:
 1. 8-count carton (berries 'n' cream)
 2. 25-count carton (berries 'n' cream)
 3. 50-count carton (berries 'n' cream)
 4. 50x1 unit dose (sample) dispenser carton (berries 'n' cream)
 5. 8-count carton (cool mint)
 6. 25-count carton (cool mint)
 7. 50-count carton (cool mint)
 8. 50x1 unit dose (sample) dispenser carton (cool mint)
 9. 8-count carton (tropical fruit)
 10. 25-count carton (tropical fruit)
 11. 50-count carton (tropical fruit)

- b) Immediate Container Labels
 - 1.1-count sample pouch (berries 'n' cream)
 - 2.1-count pouch (berries 'n' cream)
 - 3.25- count bottle label (berries 'n' cream)
 - 4.50- count bottle label (berries 'n' cream)
 - 5.1-count sample pouch (cool mint)
 - 6.1- count pouch (cool mint)
 - 7.25- count bottle label (cool mint)
 - 8.50- count bottle label (cool mint)
 - 9.1-count pouch (tropical fruit)
 - 10. 25-count bottle label (tropical fruit)
 - 11. 50-count bottle label (tropical fruit)

The final printed labeling (FPL) must be formatted in accordance with the requirements of 21 CFR 201.66.

We remind you to remove the flag "New!" from the labels and labeling six months after introduction into the marketplace.

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 20-801/S-012.**" 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
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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

NDA 20-801/S-012

Page 3

If you have any questions, call Geri Smith, Regulatory Project Manager, at (301) 796-2204.

Sincerely,

{See appended electronic signature page}

Joel Schiffenbauer, MD
Deputy Director
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

Enclosure

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

/s/

Joel Schiffenbauer
12/17/2007 07:29:26 AM

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-801/S-012

LABELING



MAXIMUM STRENGTH
Pepcid^{AC}
EZ CHEWS
Cool Mint Flavor
Chewable Tablets

NEW!

MAXIMUM STRENGTH

Pepcid^{AC}
Famotidine Tablets 20 mg
Acid Reducer

EZ CHEWS
Can take without water!

Just One Tablet!
Prevents & Relieves Heartburn
Due to Acid Indigestion

25 Cool Mint Flavor
Chewable Tablets

AC TABLET

MAXIMUM STRENGTH

Pepcid^{AC}

EZ CHEWS

Can take without water!

Just One Tablet!

Prevents & Relieves Heartburn
Due to Acid Indigestion

25 Cool Mint Flavor
Chewable Tablets

AC TABLET

Drug Facts (continued)

Warnings

- Do not use if you are allergic to famotidine or other acid reducers.
- Do not use if you are allergic to certain food and beverages.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.

Precautions

- Do not use if you are allergic to famotidine or other acid reducers.
- Do not use if you are allergic to certain food and beverages.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.

Side Effects

- Do not use if you are allergic to famotidine or other acid reducers.
- Do not use if you are allergic to certain food and beverages.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.

Interactions

- Do not use if you are allergic to famotidine or other acid reducers.
- Do not use if you are allergic to certain food and beverages.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.

Contraindications

- Do not use if you are allergic to famotidine or other acid reducers.
- Do not use if you are allergic to certain food and beverages.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.

Warnings (continued)

- Do not use if you are allergic to famotidine or other acid reducers.
- Do not use if you are allergic to certain food and beverages.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.

Precautions (continued)

- Do not use if you are allergic to famotidine or other acid reducers.
- Do not use if you are allergic to certain food and beverages.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.

Side Effects (continued)

- Do not use if you are allergic to famotidine or other acid reducers.
- Do not use if you are allergic to certain food and beverages.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.
- Do not use if you are taking famotidine or other acid reducers.

Interactions (continued)

- Do not use if you are allergic to famotidine or other acid reducers.
- Do not use if you are allergic to certain food and beverages.
- Do not use if you are taking famotidine or other acid reducers.
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- Do not use if you are taking famotidine or other acid reducers.

Contraindications (continued)

- Do not use if you are allergic to famotidine or other acid reducers.
- Do not use if you are allergic to certain food and beverages.
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MAXIMUM STRENGTH

Pepcid^{AC}

EZ CHEWS
can take without water!

50 Cool Mint Flavor Chewable Tablets

NEW!

MAXIMUM STRENGTH

Pepcid^{AC}

EZ CHEWS
can take without water!

Just One Tablet!
Prevents & Relieves Heartburn
Due to Acid Indigestion

50 Cool Mint Flavor Chewable Tablets

AC 14-01-2001

Drug Facts (continued)

Warnings

- Do not use if you are pregnant or nursing.
- Do not use if you are taking other acid reducers.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.

Precautions

- Do not use if you are pregnant or nursing.
- Do not use if you are taking other acid reducers.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.

Directions

- Do not use if you are pregnant or nursing.
- Do not use if you are taking other acid reducers.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.

Other Information

- Do not use if you are pregnant or nursing.
- Do not use if you are taking other acid reducers.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.

Keep this and all other medications out of the reach of children.

Drug Facts (continued)

Warnings

- Do not use if you are pregnant or nursing.
- Do not use if you are taking other acid reducers.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.

Precautions

- Do not use if you are pregnant or nursing.
- Do not use if you are taking other acid reducers.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.

Directions

- Do not use if you are pregnant or nursing.
- Do not use if you are taking other acid reducers.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.
- Do not use if you are taking other drugs that may interact with this product.

Other Information

- Do not use if you are pregnant or nursing.
- Do not use if you are taking other acid reducers.
- Do not use if you are taking other drugs that may interact with this product.
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Keep this and all other medications out of the reach of children.

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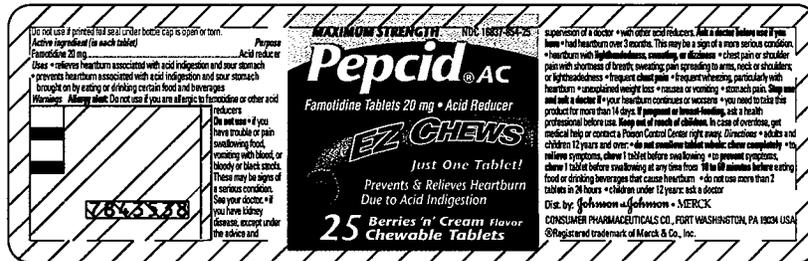
Keep this and all other medications out of the reach of children.

Blister @ 100% Scale



Blister @ 200% Scale





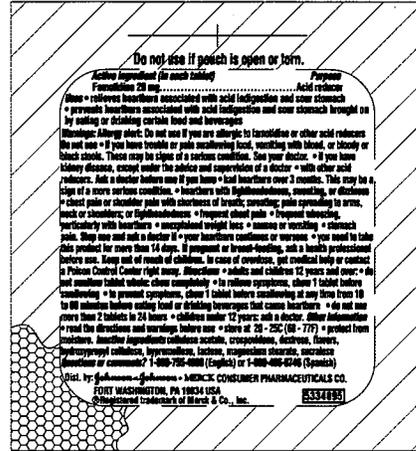
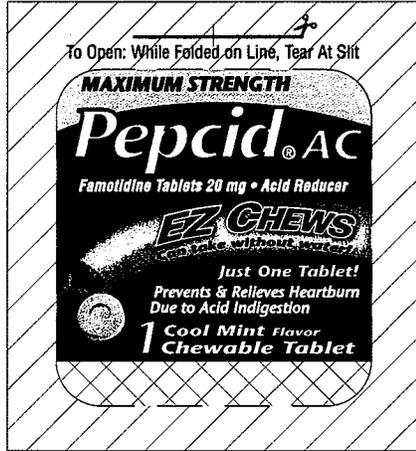
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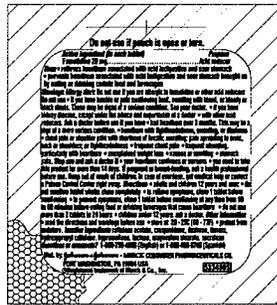
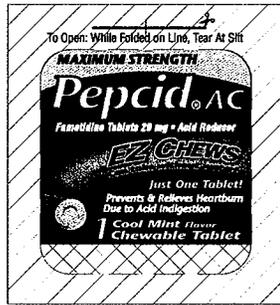
<p>Do not use if printed foil seal under bottle cap is open or torn. Active ingredient (in each tablet) Famotidine 20 mg Purpose Acid reducer Uses • relieves heartburn associated with acid indigestion and sour stomach • prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain food and beverages Warnings • Allergy alert: Do not use if you are allergic to famotidine 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. • if you have kidney disease, except under the advice and supervision of a doctor • with other acid reducers</p> <p>LOT: EXP: 7843539</p>	<p>MAXIMUM STRENGTH NDC 16937-854-50 Pepcid[®] AC Famotidine Tablets 20 mg • Acid Reducer EZ CHEWS Just One Tablet! Prevents & Relieves Heartburn Due to Acid Indigestion 50 Berries 'n' Cream Flavor Chewable Tablets</p>	<p>Ask a doctor before use if you have • had heartburn over 3 months. This may be a sign of a more serious condition. • heartburn with light-headedness, sweating, or dizziness • chest pain or shoulder pain with shortness of breath, sweating, pain spreading to arms, neck or shoulder; or lightheadedness • frequent chest pain • frequent wheezing, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. 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 • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before eating or drinking • to prevent symptoms, chew 1 tablet before eating or drinking • if you have symptoms that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor Dist. by: Johnson & Johnson • MERCK CONSUMER PHARMACEUTICALS CO., FORT WASHINGTON, PA 19044 USA ©Registered trademark of Merck & Co., Inc.</p>
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150% ACTUAL SIZE

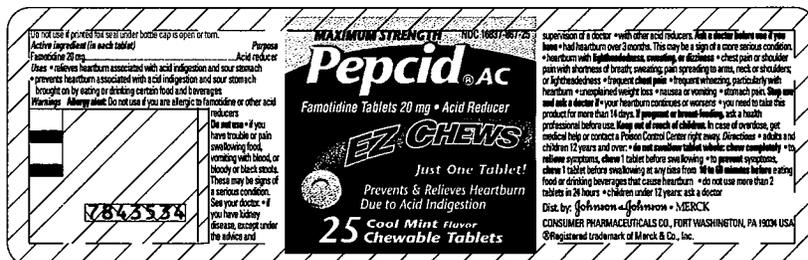


Blister @ 100% Scale

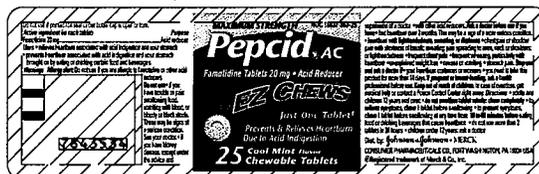


Blister @ 200% Scale





150% ACTUAL SIZE



Do not use if primed foil seal under bottle cap is open or torn.
 Active ingredient (in each tablet): Famotidine 20 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 food and beverages.
 Warnings: Allergy alert: Do not use if you are allergic to famotidine 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. If you have kidney disease, except under the advice and supervision of a doctor, with other acid reducers.

MAXIMUM STRENGTH NDC 18227-007-50
Pepcid[®] AC
 Famotidine Tablets 20 mg • Acid Reducer
EZ CHEWS
 Just One Tablet!
 Prevents & Relieves Heartburn Due to Acid Indigestion
50 Cool Mint flavor Chewable Tablets

Ask a doctor before use if you have: had heartburn over 3 months. This may be a sign of a more serious condition. • heartburn with light-headedness, sweating, or dizziness • chest pain or shoulder pain with shortness of breath, sweating, pain spreading to arms, neck or shoulder, or lightheadedness • frequent chest pain • frequent wheezing, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. See your 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: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before or following • to prevent symptoms, chew 1 tablet before awakening at any time from 10 to 16 hours before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor.
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150% ACTUAL SIZE

Do not use if primed foil seal under bottle cap is open or torn.
 Active ingredient (in each tablet): Famotidine 20 mg.
 Purpose: Acid reducer.
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 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. If you have kidney disease, except under the advice and supervision of a doctor, with other acid reducers.

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Blister @ 100% Scale



Blister @ 200% Scale



Do not use if peptic ulcers under before cap is open or torn.
Active ingredient (in each tablet)
 Famotidine 20 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 food and beverages
Warnings • **Always** about Do not use if you are allergic to famotidine or other acid reducers
 • Do not use if you have trouble swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor if you have kidney disease, except under the advice and

MAXIMUM STRENGTH NDC 1047-2003-25

Pepcid[®] AC

Famotidine Tablets 20 mg • Acid Reducer

EZ CHEWS

Just One Tablet!

Prevents & Relieves Heartburn Due to Acid Indigestion

25 Tropical Fruit Flavor Chewable Tablets

supervision of a doctor • with other acid reducers. **Ask a doctor before use if you have** • had heartburn over 2 months. This may be a sign of a more serious condition.
 • heartburn with nighttime awakenings, vomiting, or diarrhea • chest pain or shoulder pain with shortness of breath, sweating, pain spreading to arms, neck or shoulder, or lightheadedness • frequent chest pain • frequent retching, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. **Do not use and ask a doctor if you have** heartburn conditions or warning • 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: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before swallowing at any time from 30 to 60 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor
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LOT: 7843542

EXP:

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Do not use if peptic ulcers under before cap is open or torn.
Active ingredient (in each tablet)
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Purpose
 Acid reducer
Uses • relieves heartburn associated with acid indigestion and sour stomach
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MAXIMUM STRENGTH NDC 1047-2003-25

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Famotidine Tablets 20 mg • Acid Reducer

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LOT: 7843542

EXP:

<p>Do not use if printed foil seal under bottle cap is open or torn. Active ingredient (in each tablet) Purpose Famotidine 20 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 food and beverages Warnings Allergy alert: Do not use if you are allergic to famotidine 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. • if you have kidney disease, except under the advice and supervision of a doctor • with other acid reducers</p> <p>LOT: _____ EXP: _____ 7843543</p>	<p>MAXIMUM STRENGTH NDC 10827-0453-50</p> <h1>Pepcid[®] AC</h1> <p>Famotidine Tablets 20 mg • Acid Reducer</p> <h2>EZ CHEWS</h2> <p>Just One Tablet! Prevents & Relieves Heartburn Due to Acid Indigestion</p> <h3>50 Tropical Fruit Flavor Chewable Tablets</h3>	<p>Ask a doctor before use if you have • had heartburn over 3 months. This may be a sign of a more serious condition. • heartburn with lightheadedness, weakness, or dizziness • chest pain or shoulder pain with shortness of breath, sweating, pain spreading to arms, neck or shoulder, or lightheadedness • frequent chest pain • frequent vomiting, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. 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: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before swallowing at any time from 10 to 60 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor Div. by: Johanson-Johnson • MERCK CONSUMER PHARMACEUTICALS CO., FORT WASHINGTON, PA 19034 USA ©Registered trademark of Merck & Co., Inc.</p>
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150% ACTUAL SIZE

<p>Do not use if printed foil seal under bottle cap is open or torn. Active ingredient (in each tablet) Purpose Famotidine 20 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 food and beverages Warnings Allergy alert: Do not use if you are allergic to famotidine 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. • if you have kidney disease, except under the advice and supervision of a doctor • with other acid reducers</p> <p>LOT: _____ EXP: _____ 7843543</p>	<p>MAXIMUM STRENGTH NDC 10827-0453-50</p> <h1>Pepcid[®] AC</h1> <p>Famotidine Tablets 20 mg • Acid Reducer</p> <h2>EZ CHEWS</h2> <p>Just One Tablet! Prevents & Relieves Heartburn Due to Acid Indigestion</p> <h3>50 Tropical Fruit Flavor Chewable Tablets</h3>	<p>Ask a doctor before use if you have • had heartburn over 3 months. This may be a sign of a more serious condition. • heartburn with lightheadedness, weakness, or dizziness • chest pain or shoulder pain with shortness of breath, sweating, pain spreading to arms, neck or shoulder, or lightheadedness • frequent chest pain • frequent vomiting, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. 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: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before swallowing at any time from 10 to 60 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor Div. by: Johanson-Johnson • MERCK CONSUMER PHARMACEUTICALS CO., FORT WASHINGTON, PA 19034 USA ©Registered trademark of Merck & Co., Inc.</p>
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**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-801/S-012

MEDICAL REVIEW(S)



CENTER FOR DRUG EVALUATION AND RESEARCH
Division of Nonprescription Clinical Evaluation
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002
301.796.2280

MEMORANDUM

Date: December 17, 2007

From: Joel Schiffenbauer, M.D.
Deputy Director, DNCE

Subject: NDA 20-801 (s012), Pepcid AC EZ Chews

Sponsor: Merck

Background:

Pepcid AC (famotidine 10 mg) and Maximum Strength Pepcid AC (famotidine 20 mg), have been available without a prescription for the prevention and treatment of heartburn. The 10-mg product is available in several different dosage forms (film-coated tablet, gelcap, and chewable tablet). The 20-mg famotidine product is available only as a film-coated tablet (FCT).

This application was filed as a supplement to the original Pepcid AC Chewable Tablets NDA (NDA 20-801) and the original 10-mg formulation has been discontinued. The new 20-mg formulation will replace it as the only chewable tablet formulation under NDA 20-801.

The clinical pharmacology review was performed by Dr. T. Ghosh; the chemistry review was performed by Dr. S. Kelly; and the labeling review was performed by Dr. R. Tan. The reader is referred to the original reviews for more details.

Toxicology:

No new data presented.

Clinical Pharmacology:

A bioequivalence study (Study 144) to compare the new 20-mg chewable tablet formulation to the reference product 20-mg film-coated tablet was conducted and demonstrated that the new formulation is bioequivalent to the reference standard film coated tablet, with and without water. The summary results are provided in tables in the appendix.

The clinical pharmacology reviewer provided the following comments with which I agree:

The study concluded that:

- 1. Famotidine 20-mg chewable tablet without water and famotidine 20-mg filmcoated tablet with water are bioequivalent with respect to AUC and C_{max} .*
- 2. Famotidine 20-mg chewable tablet with water and famotidine 20-mg film-coated tablet with water are bioequivalent with respect to AUC and C_{max} .*
- 3. Famotidine 20-mg chewable tablets taken without water and with water and famotidine 20-mg film-coated tablets taken with water were generally well tolerated in this study.*

Chemistry:

The chemistry reviewer provides the following comments with which I agree:

Adequate CMC data is provided. Included is six months of accelerated and room temperature stability data for five lots of chewable tablets manufactured at the commercial scale with the proposed formulation (3 batches of Berries 'n' Cream flavor, 1 batch of Cool Mint flavor, and 1 batch of Tropical Fruit flavor). The stability data supports the 36-month expiry date and storage conditions currently approved for the 10 mg chewable dose.

Efficacy:

Efficacy was not assessed in this development program. Efficacy of the 20-mg dose was established in the sNDA for Maximum Strength Pepcid AC (NDA 20-325/S-015, approved 9/23/03).

Safety:

There has been extensive use of famotidine as an OTC product with no major safety concerns.

No formal clinical studies for safety were conducted in this development program. In the bioequivalence study, nine subjects reported clinical adverse experiences. None of the adverse experiences were serious, none were unexpected and no subject withdrew from the study due to an adverse experience. All adverse experiences resolved.

Therefore, there are no new safety concerns raised by this submission.

Pediatrics:

This submission does not trigger PREA as there is no new formulation (the RLD and the new product are both tablets).

Labeling:

The labeling reviewer comments:

The labeling submitted in this application is acceptable. However, the sponsor should be reminded that the word "New!" must be removed from the principal display panels of carton labels after 180 days of OTC marketing.

I agree.

Conclusions:

The applicant has demonstrated that the new EZ Chew formulation is bioequivalent to the original 20 mg famotidine tablets. The applicant has demonstrated that the product can be taken with or without water and the pharmacokinetic characteristics will not be significantly altered. There are no chemistry issues. There are no labeling issues.

Recommendations:

It is recommended that this NDA be approved. The use of the word "new" on the label should be removed after 6 months.

APPENDIX

Comparison of Mean Famotidine AUC_{0-∞} and C_{max} Values Following Administration of 20-mg Single Oral Doses of the FCT Taken With Water Versus 20-mg of the CT Taken With or Without Water to Healthy Male and Female Subjects (n=30)

Pharmacokinetic Parameter	N	Geometric Mean			Geometric Mean Ratio		MSE
		Famotidine 20 mg FCT with Water (95% CI)	Famotidine 20 mg CT without Water (95% CI)	Famotidine 20 mg CT with Water (95% CI)	CT without Water / FCT (90% CI)	CT with Water / FCT (90% CI)	
AUC _{0-∞} (ng/mL·hr)	30	394.8 (347.6, 448.4)	398.5 (350.9, 452.6)	440.1 (387.5, 499.8)	1.01 (0.94, 1.09)	1.11 (1.04, 1.20)	0.029
C _{max} (ng/mL)	30	65.1 (56.9, 74.5)	67.2 (58.7, 76.9)	73.0 (63.8, 83.6)	1.03 (0.93, 1.14)	1.12 (1.02, 1.24)	0.053

Geometric Means based on least square estimates from an ANOVA performed on natural log-transformed values
MSE=Mean Square Error on log scale
Test for Carryover Effect was non-significant: AUC_{0-∞} p-value= 0.996, C_{max} p-value= 0.551

Comparison of Mean Famotidine T_{max} and t_{1/2} Values Following Administration of 20-mg Single Oral Doses of the FCT Taken With Water Versus 20-mg of the CT Taken With or Without Water to Healthy Male and Female Subjects (n=30)

Pharmacokinetic Parameter	N	Treatment Statistics			Median Treatment Differences	
		Famotidine 20 mg FCT with Water	Famotidine 20 mg CT without Water	Famotidine 20 mg CT with Water	CT without Water - FCT (95% CI)	CT with Water - FCT (95% CI)
T _{max} (hr)	30	1.50	1.50	1.25	0.00 (-0.25, 0.50)	0.00 (-0.50, 0.25)
t _{1/2} (hr)	30	4.24	4.43	4.26	0.13 (-0.56, 0.74)	-0.03 (-0.64, 0.45)

Harmonic means are report for t_{1/2} treatment statistics. Medians are report for T_{max} treatment statistics.
Median treatment differences and confidence intervals are based on Hodges-Lehmann estimates.

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/s/

Joel Schiffenbauer
12/17/2007 07:29:01 AM
MEDICAL OFFICER

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-801/S-012

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW		
1. ORGANIZATION CDER/ONDQA Division of Post-Marketing Evaluation HFD-590		2. NDA # 20-801 Original NDA approved:
3. NAME AND ADDRESS OF APPLICANT Merck & Co., Inc. Sumneytown Pike P.O. Box 4 UN-D 129 West Point, PA 19486 Brenda McGuire, MS, RN		4. SUPPLEMENT SE2-012 23-MAR-2007 (Rec. 24-MAR-2007)
		5. Name of the Drug Pepcid AC Chewable Tablets
		6. Nonproprietary Name Famotidine
7. SUPPLEMENT PROVIDES for a new 20mg formulation of a chewable famotidine tablet; a manufacturing site change and as a consequence, a manufacturing process change; and provides for changes to the commercial container closure system		8. AMENDMENT -- SE2-012 BC 05-JUL-2007
9. PHARMACOLOGICAL CATEGORY Heartburn, Acid Indigestion	10. HOW DISPENSED OTC	11. RELATED
12. DOSAGE FORM	13. POTENCY 20 mg	
14. CHEMICAL NAME AND STRUCTURE See USAN N'-(aminosulfonyl)-3-[[[2-[(diaminomethylene)amino]-4-thiazolyl]methyl]thio] propanimidamide		
15. COMMENTS This application is submitted as an SE2 Supplement. The 20 mg famotidine chewable tablet will replace the currently approved 10 mg chewable tablet. The 20mg formula is derived from the ^{(b) (4)} as is currently used in both the PEPCID™ AC Chewable Tablet, 10mg formula, and the PEPCID™ COMPLETE Tablets (NDA 20-958, a 10mg famotidine/antacid combination). ^{(b) (4)}		
^{(b) (4)} Three chewable tablet formulations are proposed: Berries 'n' Cream, Cool Mint, and Tropical Fruit. Reference the review by Clinical Pharmacology (24-SEPT-2007). The overall EER recommendation is Acceptable (24-OCT-2007).		
16. CONCLUSIONS AND RECOMMENDATIONS Adequate CMC data is provided. Included is six months of accelerated and room temperature stability data for five lots of chewable tablets manufactured at the commercial scale with the proposed formulation (3 batches of Berries 'n' Cream flavor, 1 batch of Cool Mint flavor, and 1 batch of Tropical Fruit flavor). The stability data supports the 36-month expiry date and storage conditions currently approved for the 10 mg chewable dose. Send Comments to Sponsor. This Supplement can be Approved.		
17. REVIEWER NAME (AND SIGNATURE) Sharon Kelly, PhD R/D INITIATED BY filename: 20-801#012 NDA		DATE COMPLETED 28-SEPT-2007
DISTRIBUTION: Original: NDA 20-801#012 cc: Division File CSO Reviewer		

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this page is the manifestation of the electronic signature.**

/s/

Sharon Kelly
10/25/2007 09:55:07 AM
CHEMIST

Hasmukh Patel
10/25/2007 12:08:53 PM
CHEMIST

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-801/S-012

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

Clinical Pharmacology Review

PRODUCT (Generic Name):	Famotidine Chewable Tablet
PRODUCT (Proposed Brand Name):	PEPCID™ AC EZ Chews (20 mg)
NDA:	20-801 (S-012)
THERAPEUTIC CLASS:	H ₂ Blocker
PROPOSED INDICATIONS:	Prevention of Heartburn
SUBMISSION DATE:	March 23, 2007
SPONSOR:	Merck
REVIEWER:	Tapash K. Ghosh, Ph.D.
TEAM LEADER:	Sue-Chih Lee, Ph. D.
OCP DIVISION:	DCP III
OND DIVISION:	ONP

EXECUTIVE SUMMARY

This NDA supplement contains data from one bioequivalence study in healthy volunteers. Overall, the study concluded that:

1. Famotidine 20-mg chewable tablet without water and famotidine 20-mg film-coated tablet with water are bioequivalent with respect to AUC and C_{max}.
2. Famotidine 20-mg chewable tablet with water and famotidine 20-mg film-coated tablet with water are bioequivalent with respect to AUC and C_{max}.
3. Famotidine 20-mg chewable tablets taken without water and with water and famotidine 20-mg film-coated tablets taken with water were generally well tolerated in this study.

Recommendation:

The Clinical Pharmacology section of NDA 20-801 (S012) and the proposed label are acceptable. The comment below should be communicated to the Clinical Division.

Comment: The sponsor proposes a new chewable tablet strength of famotidine (PEPCID™ AC EZ Chews 20 mg), and will discontinue the currently approved PEPCID™ AC 10 mg Chewable Tablet product.

Primary Reviewer: Tapash K. Ghosh, Ph.D.
Clinical Pharmacology
Division of Clinical Pharmacology III

Team Leader: Sue-Chih Lee, Ph. D.
Div. of Clinical Pharmacology III

Background: The prevention and treatment of heartburn with medication occurs through use of both prescription and over-the-counter (OTC) drugs. PEPCID™ AC (famotidine 10 mg) and Maximum Strength PEPCID™ AC (famotidine 20 mg), an H₂-receptor antagonist (H₂RA), have been available without a prescription for the prevention and treatment of heartburn since 1995 and 2003, respectively. The 10-mg product is available in several different dosage forms (film-coated tablet, gelcap, and chewable tablet), however the 20-mg famotidine product is available only as a film-coated tablet (FCT). A chewable tablet form offers additional conveniences such as use without water, and is especially preferred by consumers who have difficulties swallowing whole tablets. It is reasonable that consumers who prefer to use the 20-mg product should have the additional choice of a chewable formulation.

This NDA supplement provides data for the new chewable tablet formulation of famotidine at a 20 mg dose, and will replace the currently approved PEPCID™ AC 10 mg Chewable Tablet product. The sponsors did not provide any explanation for this action. The trade name of "Maximum Strength PEPCID™ AC EZ Chews" has been proposed for this new product.

A bioequivalence study (Study 144) to compare the new 20-mg chewable tablet formulation to the reference product 20-mg film-coated tablet was conducted and successfully demonstrated that the new formulation is bioequivalent to the reference standard FCT, with and without water. The study concluded that:

1. Famotidine 20-mg chewable tablet without water and famotidine 20-mg film-coated tablet with water are bioequivalent with respect to AUC and C_{max}.
2. Famotidine 20-mg chewable tablet with water and famotidine 20-mg film-coated tablet with water are bioequivalent with respect to AUC and C_{max}.

- Famotidine 20-mg chewable tablets taken without water and with water and famotidine 20-mg film-coated tablets taken with water were generally well tolerated in this study.

Efficacy was not assessed in this development program. Efficacy of the 20-mg dose was established in the SNDA for Maximum Strength PEPCID AC (NDA 20-325/S-015, approved 9/23/03).

No clinical studies for safety were conducted in this development program. In the bioequivalence study (Study 144), nine subjects reported clinical adverse experiences. According to the sponsor, one of the subjects reported clinical adverse experiences that were determined by the investigator to be possibly related to study drug. None of the adverse experiences were serious, none were unexpected or newly described and no subject withdrew from the study due to an adverse experience. All adverse experiences resolved. Famotidine was found to be generally safe and well tolerated.

In order to file this application as a supplement to the original PEPCID™ AC Chewable Tablets NDA (NDA 20-801) the original 10-mg formulation has been discontinued and the new 20-mg formulation will replace it as the only chewable tablet formulation under NDA 20-801.

Product Description ; The 20mg famotidine chewable tablet formula are derived from the current PEPCID™ AC Chewable Tablet, 10mg formula. The 20mg famotidine chewable tablet formula (b) (4) as is currently used in both the PEPCID™ AC Chewable Tablet, 10mg formula, and the PEPCID™ COMPLETE Tablets (NDA 20-958, also 10mg famotidine).

The batch formula for (b) (4) is presented in the following Table. (b) (4) applies to all three flavors (Berries 'n' Cream, Cool Mint, and Tropical Fruit).

[20mg famotidine, chewable tablets] Batch Formula

Ingredient	Quantity per Unit, mg	Quantity per Batch, kg
Famotidine	20.0	(b) (4)
(b) (4)		

Draft Labeling:

The proposed labeling pertaining to clinical pharmacology are captured in the cation label shown below:



<p>MAXIMUM STRENGTH Pepcid[®] AC EZ CHEWS</p> <p>Do not use if the carton or individual pouch is open or torn.</p> <ul style="list-style-type: none"> • 1 tablet relieves heartburn due to acid indigestion • PEPCID[®] AC prevents heartburn due to acid indigestion brought on by eating and drinking certain foods and beverages. <p>The makers of Pepcid[®] AC do not manufacture store brands.</p>					
<p>Drug Facts</p> <table border="1"> <tr> <th>Active ingredient (in each tablet)</th> <th>Purpose</th> </tr> <tr> <td>Famotidine 20 mg</td> <td>Acid reducer</td> </tr> </table> <p>Uses</p> <ul style="list-style-type: none"> • 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 food and beverages <p>Warnings</p> <p>Allergy alert: Do not use if you are allergic to famotidine or other acid reducers</p> <p>Do not use</p> <ul style="list-style-type: none"> • 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. • if you have kidney disease, except under the advice and supervision of a doctor • with other acid reducers 	Active ingredient (in each tablet)	Purpose	Famotidine 20 mg	Acid reducer	<p>Drug Facts (continued)</p> <p>Ask a doctor before use if you have</p> <ul style="list-style-type: none"> • 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 • frequent chest pain • frequent wheezing, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain <p>Stop use and ask a doctor if</p> <ul style="list-style-type: none"> • your heartburn continues or worsens • you need to take this product for more than 14 days <p>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.</p>
Active ingredient (in each tablet)	Purpose				
Famotidine 20 mg	Acid reducer				
<p>Drug Facts (continued)</p> <p>Directions</p> <ul style="list-style-type: none"> • adults and children 12 years and over: <ul style="list-style-type: none"> • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before swallowing at any time from 15 to 30 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor <p>Other information</p> <ul style="list-style-type: none"> • read the directions and warnings before use • keep the carton. It contains important information. 	<p>Drug Facts (continued)</p> <ul style="list-style-type: none"> • store at 20° - 25°C (68° - 77°F) • protect from moisture <p>Inactive ingredients</p> <p>cellulose acetate, croscarmellose, D&C red #7 calcium lake, dextrose, FD&C blue #1 aluminum lake, FD&C red #40 aluminum lake, flavors, hydroxypropyl cellulose, hypromellose, lactose, magnesium stearate, sucralose</p> <p>Questions or comments?</p> <p>1-800-715-4969 (English) or 1-800-465-4746 (Spanish)</p>				

The proposed trade name “Maximum Strength PEPCID™ AC EZ Chews” is a combination of the FDA-approved brand name for the 20-mg film-coated tablet (FCT) product (Maximum Strength PEPCID™ AC, NDA 20-325/S-015, approved 9/23/03), and the term ‘EZ Chews’ which relates specifically to the new chewable formulation.

The Drug Facts label for Maximum Strength PEPCID™ AC EZ Chews (“EZ Chews”) has been created by taking the approved PEPCID™ AC Chewable Tablets (10 mg) Drug Facts label as a “base” label, and adding to it selected elements of the Maximum Strength

PEPCID™ AC Film-Coated Tablets (NDA 20-325) label that are relevant to a 20-mg product.

The statements extracted from the Maximum Strength PEPCID™ AC FCT label (NDA 20-325/S-015, approved 9/23/03) and incorporated into the proposed EZ Chews label are:

- In the **Do not use** section, the bullet stating “*if you have kidney disease, except under the advice and supervision of a doctor*”.
- In the **Directions** section, the timeframe associated with heartburn prevention with a 20-mg famotidine product (approved for Maximum Strength PEPCID™ AC FCT): “*to prevent symptoms, chew 1 tablet before swallowing at any time from 10 to 60 minutes before eating food or drinking beverages that cause heartburn*”.

Several additional modifications were made to the proposed package/label which are relevant to the new EZ Chews formulation, including the following pertinent to clinical pharmacology:

- The text and artwork on the principal display panel are consistent with currently approved packaging for the entire PEPCID OTC product line with the exception of the phrase “**Can take without water**”. This phrase has been added to the front panel of the EZ Chews package to make consumers aware of this feature of the product while at the point of purchase, and is substantiated by the results of the bioequivalence Study 144.

The above modification is acceptable from clinical pharmacology perspective.

Review of Study 144:

NDA: 20-801/SE 012/Study 144

Study Dates: 8/19/06 – 8/31/06

A Single-dose, open-label, three-period crossover study to assess the bioequivalence of famotidine 20-mg film-coated tablets with water compared to famotidine 20-mg chewable tablets (CT) without water and famotidine 20-mg ct (CTw) with water

OBJECTIVE(S): *Primary Objective:* To assess the bioequivalence of a single dose of 20-mg famotidine CT taken without water compared with a single dose of 20-mg famotidine FCT taken with water. *Secondary: Objective:* To assess the bioequivalence of a single dose of 20-mg famotidine CT taken with water compared with a single dose of famotidine 20-mg FCT taken with water.

STUDY DESIGN: This was an open-label, single dose, randomized, three-period crossover study where thirty (30) healthy male and female subjects [Male (n =, 16 with age range 18-37 yrs); Female (n = 14 with age range 19-39 yrs)] received each of the 3

treatments in a randomized manner: 20-mg FCT with water; 20-mg CT without water and 20-mg CTw with water. Following a single dose of each treatment, subjects were confined to the study unit for at least 24 hours for plasma collection. Each treatment period was separated by 5 to 7 days. The duration of the entire study was approximately 6 weeks.

Human plasma samples were analyzed for famotidine concentrations. The analytical method for the determination of famotidine in human plasma involves isolation, via liquid-liquid extraction, of the analyte and internal standard from plasma, followed by HPLC-MS/MS analysis. The lower limit of quantitation (LLOQ) for the plasma assay was 1.00 ng/mL and the linear calibration range was 1.00 to 500 ng/mL.

RESULTS: Pharmacokinetics: All 30 subjects who entered and completed the 3 study periods were included in the analyses. The results are summarized below:

Comparison of Mean Famotidine AUC_{0-∞} and C_{max} Values Following Administration of 20-mg Single Oral Doses of the FCT Taken With Water Versus 20-mg of the CT Taken With or Without Water to Healthy Male and Female Subjects (n=30)

Pharmacokinetic Parameter	N	Geometric Mean			Geometric Mean Ratio		MSE
		Famotidine 20 mg FCT with Water (95% CI)	Famotidine 20 mg CT without Water (95% CI)	Famotidine 20 mg CT with Water (95% CI)	CT without Water / FCT (90% CI)	CT with Water / FCT (90% CI)	
AUC _{0-∞} (ng/mL hr)	30	394.8 (347.6, 448.4)	398.5 (350.9, 452.6)	440.1 (387.5, 499.8)	1.01 (0.94, 1.09)	1.11 (1.04, 1.20)	0.029
C _{max} (ng/mL)	30	65.1 (56.9, 74.5)	67.2 (58.7, 76.9)	73.0 (63.8, 83.6)	1.03 (0.93, 1.14)	1.12 (1.02, 1.24)	0.053

Geometric Means based on least square estimates from an ANOVA performed on natural log-transformed values
MSE=Mean Square Error on log scale
Test for Carryover Effect was non-significant: AUC_{0-∞} p-value= 0.996, C_{max} p-value= 0.551

Individual Famotidine AUC_{0-∞} and C_{max} Values and Summary Statistics Following Administration of 20-mg Single Oral Doses of the FCT Taken With Water Versus 20-mg of the CT Taken With or Without Water to Healthy Male and Female Subjects

Allocation Number	AUC _{0-∞} (ng/mL·hr)					C _{max} (ng/mL)				
	Trr A	Trr B	Trr C	B/A Ratio	C/A Ratio	Trr A	Trr B	Trr C	B/A Ratio	C/A Ratio
1	329.20	366.00	346.60	1.11	1.05	68.90	60.50	61.90	0.88	0.90
2	351.60	371.60	368.70	1.63	1.05	47.20	58.80	53.70	1.25	1.14
3	846.40	899.00	821.90	1.06	0.97	145.00	149.00	115.00	1.03	0.79
4	287.20	223.30	277.30	0.78	0.97	38.40	33.90	43.10	0.88	1.12
5	623.40	657.90	505.30	1.06	0.81	100.00	91.20	81.80	0.91	0.82
6	377.00	363.20	323.40	0.97	0.86	67.40	67.70	56.30	1.00	0.84
7	532.90	342.20	366.70	0.64	1.06	57.20	67.00	81.00	1.17	1.42
8	399.50	603.10	465.40	1.51	1.16	54.30	96.30	62.70	1.77	1.15
9	502.30	440.80	440.10	0.88	0.88	75.40	81.70	69.30	1.08	0.92
10	492.10	303.90	359.60	1.02	1.14	108.00	78.30	88.40	0.73	0.82
11	365.90	348.20	399.90	0.95	1.09	60.30	64.80	70.30	1.07	1.17
12	497.40	385.30	343.00	0.77	1.09	62.70	56.10	61.40	0.89	0.98
13	517.00	785.30	817.30	1.52	1.58	59.40	127.00	146.00	2.14	2.46
14	316.00	458.70	403.20	1.45	1.28	58.30	68.30	76.10	1.17	1.31
15	410.80	340.50	313.50	1.32	1.25	79.00	75.40	92.30	0.93	1.17
16	236.60	251.20	427.00	1.06	1.80	36.60	43.80	64.90	1.20	1.77
17	255.60	207.80	250.90	0.81	0.98	54.40	38.70	44.10	0.71	0.81
18	331.60	262.20	391.20	0.79	1.18	62.50	47.10	70.00	0.75	1.12
19	640.40	641.70	614.80	1.00	0.96	97.30	110.00	93.10	1.13	0.96
20	370.60	361.90	641.30	0.98	1.73	57.90	55.90	147.00	0.97	2.54
21	223.10	319.80	324.50	1.43	1.45	31.40	51.40	42.30	1.64	1.35
22	214.90	237.00	265.80	1.10	1.24	36.30	41.30	47.80	1.14	1.32
23	309.80	317.00	300.20	1.02	0.97	51.20	71.10	54.90	1.39	1.07
24	317.80	282.00	285.00	0.89	0.90	42.00	55.00	50.90	1.31	1.21
25	326.60	335.70	484.30	1.03	1.48	52.00	69.30	87.70	1.33	1.69
26	675.80	737.20	626.10	1.09	0.93	161.00	121.00	106.00	0.75	0.66
27	383.70	264.20	442.00	0.68	1.14	90.70	38.80	107.00	0.43	1.18
28	421.70	434.30	321.20	1.03	1.24	80.70	100.00	81.10	1.24	1.60
29	429.30	338.20	483.80	0.79	1.13	72.80	50.50	77.40	0.69	1.06
30	526.30	412.40	429.70	0.78	0.82	104.00	89.00	80.10	0.86	0.77
Arithmetic Mean	417.25	429.79	461.40			70.41	71.96	77.12		
Standard Deviation	146.12	177.79	146.77			30.39	28.23	26.94		
Median	382.85	365.60	441.05			61.40	67.35	73.20		
Geometric Mean	394.83	398.51	440.07	1.01	1.11	65.09	67.15	73.05	1.03	1.12

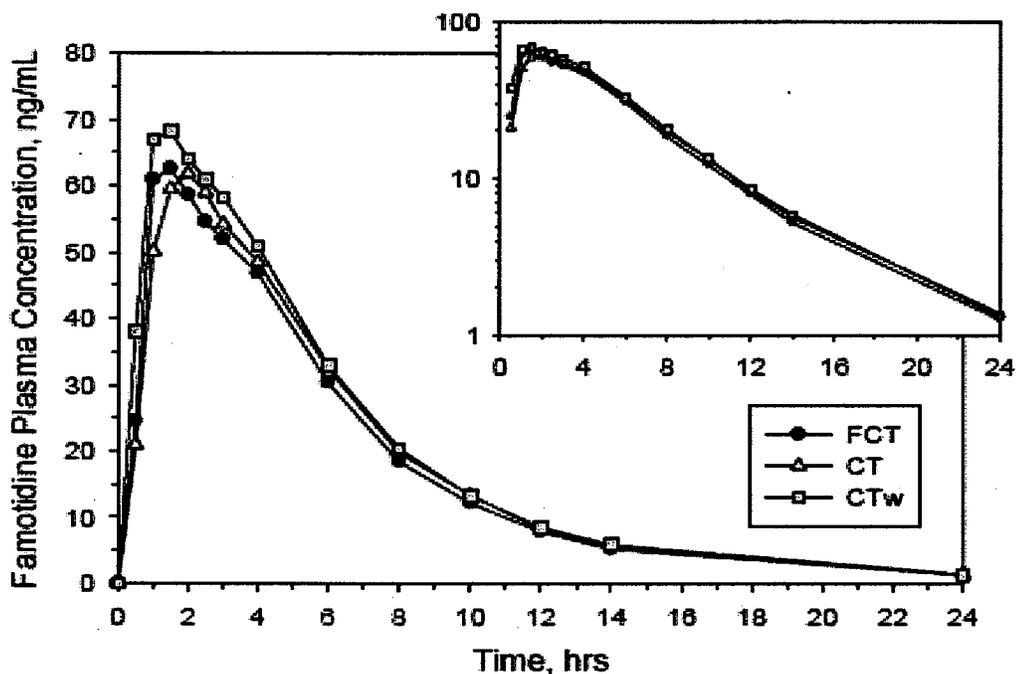
Treatment A = Famotidine 20 mg FCT with Water
 Treatment B = Famotidine 20 mg CT without Water
 Treatment C = Famotidine 20 mg CT with Water
 Geometric Means based on least square estimates from an ANOVA performed on natural log-transformed values

Comparison of Mean Famotidine T_{max} and t_{1/2} Values Following Administration of 20-mg Single Oral Doses of the FCT Taken With Water Versus 20-mg of the CT Taken With or Without Water to Healthy Male and Female Subjects (n=30)

Pharmacokinetic Parameter	N	Treatment Statistics			Median Treatment Differences	
		Famotidine 20 mg FCT with Water	Famotidine 20 mg CT without Water	Famotidine 20 mg CT with Water	CT without Water - FCT (95% CI)	CT with Water - FCT (95% CI)
T _{max} (hr)	30	1.50	1.50	1.25	0.00 (-0.25, 0.50)	0.00 (-0.50, 0.25)
t _{1/2} (hr)	30	4.24	4.43	4.26	0.13 (-0.56, 0.74)	-0.03 (-0.64, 0.45)

Harmonic means are report for t_{1/2} treatment statistics. Medians are report for T_{max} treatment statistics.
 Median treatment differences and confidence intervals are based on Hodges-Lehmann estimates.

**Arithmetic Mean Famotidine Plasma Concentration Profiles
Following Administration of 20-mg Single Oral Doses of the
FCT with Water (FCT), CT without Water (CT), and CT with Water (CTw)
to Healthy Male and Female Subjects
(N=30/Treatment; Inset = Semilog Scale)**



The 90% CI for the geometric mean ratio (CT/FCT and CTw/FCT) for both AUC_{0-∞} and C_{max} were within the prespecified range (0.80, 1.25), demonstrating bioequivalence of both CT and CTw with FCT. The median T_{max} and mean t_{1/2} values were also comparable.

Reviewer's comments: The BE parameters summarized in the above tables matched with this reviewer's separate analysis using WINNONLIN v 5.1.

Safety: According to the sponsor, nine (9) subjects reported clinical adverse experiences. One of the subjects reported clinical adverse experiences that were determined by the investigator to be possibly related to study drug. None of the adverse experiences were serious and no subject withdrew from the study due to an adverse experience. All adverse experiences resolved.

CONCLUSIONS: 1. Famotidine 20-mg chewable tablet without water and famotidine 20-mg filmcoated tablet with water are bioequivalent with respect to $AUC_{0-\infty}$ and C_{max} . 2. Famotidine 20-mg chewable tablet with water and famotidine 20-mg film-coated tablet with water are bioequivalent with respect to $AUC_{0-\infty}$ and C_{max} .

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

/s/

Tapash Ghosh
9/24/2007 08:47:55 AM
BIOPHARMACEUTICS

Sue Chih Lee
9/24/2007 10:03:17 AM
BIOPHARMACEUTICS

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
20-801/S-012

OTHER REVIEW(S)



OTC Drug Labeling Review for Pepcid AC “EZ Chews” Chewable Tablets

Division of Nonprescription Regulation Development • Office of Nonprescription Products
Center for Drug Evaluation and Research • Food and Drug Administration

SUBMISSION DATE:	March 23, 2007	RECEIVED DATE:	March 23, 2007
REVIEW DATE:	August 8, 2007		
NDA/SUBMISSION TYPE:	NDA 20-801/SE2-012		
PREVIOUS SUBMISSIONS	see “Background”		
SPONSOR:	Brenda McGuire, M.S., R.N. Associate Director Worldwide OTC Regulatory Affairs Merck Research Laboratories 484-344-7235		
DRUG PRODUCT(S):	Pepcid AC Chewable Tablets		
ACTIVE INGREDIENT:	Famotidine, 10 mg or 20 mg (Maximum Strength)		
PHARMACOLOGICAL CATEGORY:	acid reducer		
LABELING SUBMITTED:	Carton labels 1. 8-ct carton (berries ‘n’ cream) 2. 25-ct carton (berries ‘n’ cream) 3. 50-ct carton (berries ‘n’ cream) 4. 50x1 dispensit (berries ‘n’ cream) 5. 8-ct carton (cool mint) 6. 25-ct carton (cool mint) 7. 50-ct carton (cool mint) 8. 50x1 dispensit (cool mint) 9. 8-ct carton (tropical fruit) 10. 25-ct carton (tropical fruit) 11. 50-ct carton (tropical fruit) Container labels 12. 1-ct sample pouch (berries ‘n’ cream) 13. 1-ct trade pouch (berries ‘n’ cream) 14. 25-ct bottle label (berries ‘n’ cream) 15. 50-ct bottle label (berries ‘n’ cream) 16. 1-ct sample pouch (cool mint) 17. 1-ct trade pouch (cool mint) 18. 25-ct bottle label (cool mint) 19. 50-ct bottle label (cool mint) 20. 1-ct trade pouch (tropical fruit)		

	21. 25-ct bottle label (tropical fruit) 22. 50-ct bottle label (tropical fruit)
REVIEWER:	Reynold Tan
TEAM LEADER:	Helen Cothran

Background:

The sponsor submitted this application for a new 20 mg famotidine chewable tablet formulation of the Pepcid AC product line. We approved NDA 20-801/N-000 for Pepcid AC Chewable Tablets (famotidine 10 mg) on September 24, 1998 and NDA 20-325/SE2-015 for Maximum Strength Pepcid AC Film-Coated tablets (famotidine 20 mg) on September 23, 2003. At a May 22, 2006 meeting with the sponsor, we agreed that the application for the new 20 mg chewable tablet formulation should be a supplement to NDA 20-801.

This application proposes the tradename "Maximum Strength Pepcid AC EZ Chews" for the new 20 mg chewable tablet formulation. Previously, we approved the tradename "EZ Chews" for an Imodium AD chewable tablet product (NDA 20-448/SCF-004, Amendment 3, submitted September 8, 2006 and approved January 11, 2007).

Reviewer's Comment:

1. On all labels, the product is referred to using the tradename "Maximum Strength Pepcid AC EZ Chews".

Comment: The tradename "Maximum Strength Pepcid AC EZ Chews" is acceptable. We previously approved the tradename "Imodium AD EZ Chews" for another of the sponsor's products.

2. On the principal display panels of carton labels, the statement "Can take without water!" appears below the tradename "EZ Chews". The statement also appears a second time on the principal display panels of the 50-count dispensit carton labels.

Comment: This statement is acceptable.

3. The word "New!" appears on the principal display panels of carton labels.

Comment: The word "New!" must be removed from the principal display panels of carton labels after 180 days of OTC marketing.

4. Under "Directions", the following instructions are provided for adults and children 12 years and over:

- **do not swallow table whole: chew completely**
- to **relieve** symptoms, **chew** 1 tablet before swallowing
- to **prevent** symptoms, **chew** 1 tablet before swallowing at any time from **10 to 60 minutes** before eating food or drinking beverages that cause heartburn

Comment: These instructions under "Directions" are acceptable.

Reviewer's Recommendation:

The labeling submitted in this application is acceptable. However, the sponsor should be reminded that the word "New!" must be removed from the principal display panels of carton labels after 180 days of OTC marketing.

Drug Facts (continued)

Directions

- Adults and children 17 years and over:
 - do not swallow tablet whole; chew completely
 - before beginning, chew 1 tablet before swallowing
 - to prevent heartburn, chew 1 tablet before eating food or any time from 15 to 30 minutes before eating food or drinking beverages that cause heartburn
 - do not use more than 2 tablets in 24 hours
 - chewing frequency may vary
 - children under 17 years: ask a doctor

Other information

- read the directions and warnings before use
- keep the carton. It contains important information.

Directions or comments?

1-800-755-4888 (English) or 1-800-486-8746 (Spanish)

Drug Facts (continued)

Warnings

- if you have trouble or pain in swallowing food, vomiting with blood, or bloody or black stools, there may be a sign of a more serious condition, see your doctor.
- if you have taken or plan to take other acid reducers with other acid reducers
- and supervision of a doctor
- if you have taken other acid reducers, see your doctor.

Use with other acid reducers

• if you have taken or plan to take other acid reducers with other acid reducers

Warnings

- always use as directed
- if you are allergic to famotidine or other acid reducers
- if you have trouble or pain in swallowing food, vomiting with blood, or bloody or black stools, there may be a sign of a more serious condition, see your doctor.

Use with other acid reducers

- if you have taken or plan to take other acid reducers with other acid reducers
- and supervision of a doctor
- if you have taken other acid reducers, see your doctor.

Drug Facts (continued)

Warnings

- if you are allergic to famotidine or other acid reducers
- if you have trouble or pain in swallowing food, vomiting with blood, or bloody or black stools, there may be a sign of a more serious condition, see your doctor.

Use with other acid reducers

- if you have taken or plan to take other acid reducers with other acid reducers
- and supervision of a doctor
- if you have taken other acid reducers, see your doctor.

Drug Facts (continued)

Warnings

- if you are allergic to famotidine or other acid reducers
- if you have trouble or pain in swallowing food, vomiting with blood, or bloody or black stools, there may be a sign of a more serious condition, see your doctor.

Use with other acid reducers

- if you have taken or plan to take other acid reducers with other acid reducers
- and supervision of a doctor
- if you have taken other acid reducers, see your doctor.

Drug Facts (continued)

Warnings

- if you are allergic to famotidine or other acid reducers
- if you have trouble or pain in swallowing food, vomiting with blood, or bloody or black stools, there may be a sign of a more serious condition, see your doctor.

Use with other acid reducers

- if you have taken or plan to take other acid reducers with other acid reducers
- and supervision of a doctor
- if you have taken other acid reducers, see your doctor.

Drug Facts (continued)

Warnings

- if you are allergic to famotidine or other acid reducers
- if you have trouble or pain in swallowing food, vomiting with blood, or bloody or black stools, there may be a sign of a more serious condition, see your doctor.

Use with other acid reducers

- if you have taken or plan to take other acid reducers with other acid reducers
- and supervision of a doctor
- if you have taken other acid reducers, see your doctor.

Drug Facts (continued)

Warnings

- if you are allergic to famotidine or other acid reducers
- if you have trouble or pain in swallowing food, vomiting with blood, or bloody or black stools, there may be a sign of a more serious condition, see your doctor.

Use with other acid reducers

- if you have taken or plan to take other acid reducers with other acid reducers
- and supervision of a doctor
- if you have taken other acid reducers, see your doctor.

Drug Facts (continued)

Warnings

- if you are allergic to famotidine or other acid reducers
- if you have trouble or pain in swallowing food, vomiting with blood, or bloody or black stools, there may be a sign of a more serious condition, see your doctor.

Use with other acid reducers

- if you have taken or plan to take other acid reducers with other acid reducers
- and supervision of a doctor
- if you have taken other acid reducers, see your doctor.

MAXIMUM STRENGTH

Pepcid^{AC}

EZ CHEWS

25 Cool Mint Flavor Chewable Tablets

NEW!

MAXIMUM STRENGTH

Pepcid^{AC}

EZ CHEWS

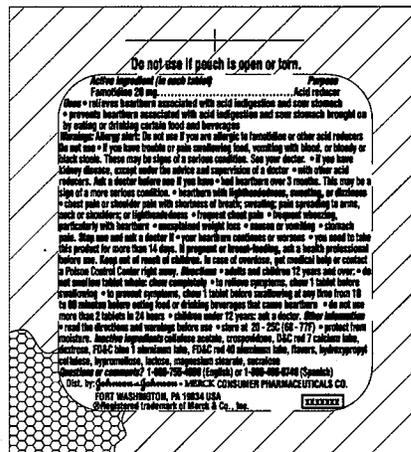
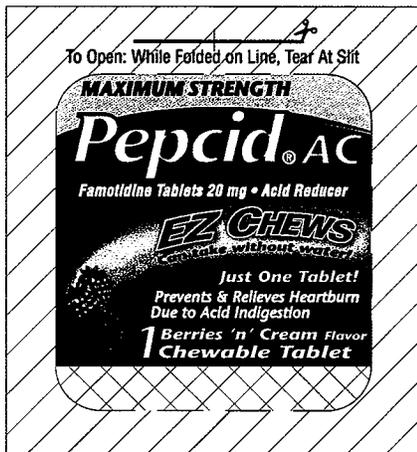
25 Cool Mint Flavor Chewable Tablets

Just One Tablet!

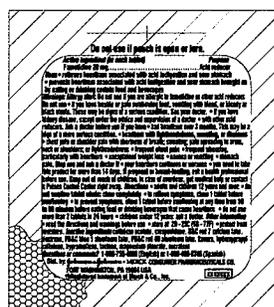
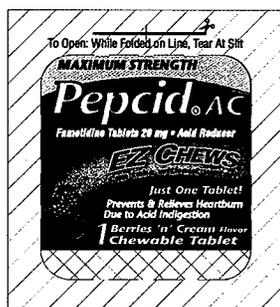
Prevents & Relieves Heartburn Due to Acid Indigestion

25 Cool Mint Flavor Chewable Tablets

ACTUAL SIZE



150% ACTUAL SIZE



Blister @ 100% Scale



Blister @ 200% Scale



Do not use if printed seal under round cap is open or torn.
 Active ingredient (in each tablet): Famotidine 20 mg. Purpose: Acid reducer.

Use: 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 food and beverages.

Warnings: Always read. Do not use if you are allergic to famotidine 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 if you have kidney disease, except under the advice of your doctor.

25 Berries 'n' Cream Flavor Chewable Tablets

Pepcid[®] AC
 Famotidine Tablets 20 mg • Acid Reducer
EZ CHEWS
 Just One Tablet!
 Prevents & Relieves Heartburn Due to Acid Indigestion

symptoms of a doctor • with other acid reducers. Ask a doctor before use if you have • had heartburn over 3 weeks. This may be a sign of a more serious condition.
 • heartburn with high blood pressure, swelling, or difficulty • chest pain or shoulder pain with shortness of breath, sweating, pain spreading to arms, neck, or shoulder, or light-headedness • frequent chest pain • frequent retching, particularly with heartburn • a unexplained weight loss • nausea or vomiting • stomach pain. 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: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before eating • to prevent symptoms, chew 1 tablet before eating at any time from 10 am till bedtime before eating food or drinking beverages that cause heartburn. • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor.)

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 ©Registered trademark of Merck & Co., Inc.

150% ACTUAL SIZE

Do not use if printed seal under round cap is open or torn.
 Active ingredient (in each tablet): Famotidine 20 mg. Purpose: Acid reducer.

Use: 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 food and beverages.

Warnings: Always read. Do not use if you are allergic to famotidine 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 if you have kidney disease, except under the advice of your doctor.

25 Berries 'n' Cream Flavor Chewable Tablets

Pepcid[®] AC
 Famotidine Tablets 20 mg • Acid Reducer
EZ CHEWS
 Just One Tablet!
 Prevents & Relieves Heartburn Due to Acid Indigestion

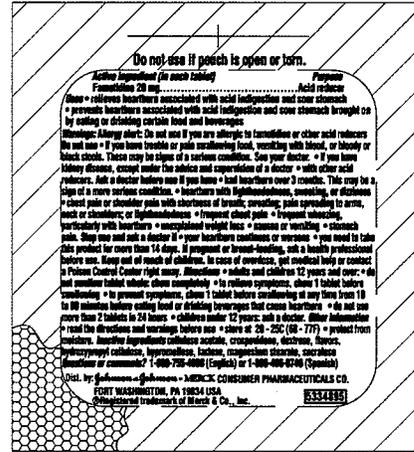
symptoms of a doctor • with other acid reducers. Ask a doctor before use if you have • had heartburn over 3 weeks. This may be a sign of a more serious condition.
 • heartburn with high blood pressure, swelling, or difficulty • chest pain or shoulder pain with shortness of breath, sweating, pain spreading to arms, neck, or shoulder, or light-headedness • frequent chest pain • frequent retching, particularly with heartburn • a unexplained weight loss • nausea or vomiting • stomach pain. 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: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before eating • to prevent symptoms, chew 1 tablet before eating at any time from 10 am till bedtime before eating food or drinking beverages that cause heartburn. • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor.)

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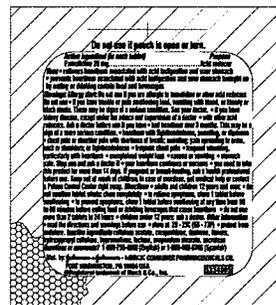
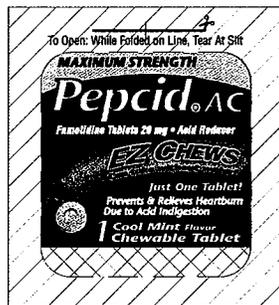
<p>Do not use if printed foil seal under bottle cap is open or torn. Active ingredient (in each tablet) Famotidine 20 mg</p> <p>Purpose Acid Reducer</p> <p>Uses • relieves heartburn associated with acid indigestion and sour stomach • prevents heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain food and beverages</p> <p>Warnings • Allergy alert: Do not use if you are allergic to famotidine or other acid reducers</p> <p>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. • if you have kidney disease, except under the advice and supervision of a doctor • with other acid reducers</p> <p>LOT:</p> <p>EXP:</p> <p style="text-align: center;">7843339</p>	<p>MAXIMUM STRENGTH <small>NO. 10037-054-01</small></p> <h1 style="margin: 0;">Pepcid[®] AC</h1> <p style="margin: 0;">Famotidine Tablets 20 mg • Acid Reducer</p> <h2 style="margin: 0;">EZ CHEWS</h2> <p style="margin: 0;">Just One Tablet!</p> <p style="margin: 0;">Prevents & Relieves Heartburn Due to Acid Indigestion</p> <h3 style="margin: 0;">50 Berries 'n' Cream Flavor Chewable Tablets</h3>	<p>Ask a doctor before use if you have • 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 • frequent chest pain • frequent vomiting, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. Stop use and ask a doctor if • your heartburn continues or worsens • you need to take this product for more than 14 days</p> <p>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.</p> <p>Directions • adults and children 12 years and over: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before eating/drinking at any time from 10 to 60 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor</p> <p>Dist. by: Johnson & Johnson • MERCK CONSUMER PHARMACEUTICALS CO., FORT WASHINGTON, PA 19028 USA ©Registered trademark of Merck & Co., Inc.</p>
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150% ACTUAL SIZE

<p>Do not use if printed foil seal under bottle cap is open or torn. Active ingredient (in each tablet) Famotidine 20 mg</p> <p>Purpose Acid Reducer</p> <p>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 food and beverages</p> <p>Warnings • Allergy alert: Do not use if you are allergic to famotidine or other acid reducers</p> <p>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. • if you have kidney disease, except under the advice and supervision of a doctor • with other acid reducers</p> <p>LOT:</p> <p>EXP:</p> <p style="text-align: center;">7843339</p>	<p>MAXIMUM STRENGTH <small>NO. 10037-054-01</small></p> <h1 style="margin: 0;">Pepcid[®] AC</h1> <p style="margin: 0;">Famotidine Tablets 20 mg • Acid Reducer</p> <h2 style="margin: 0;">EZ CHEWS</h2> <p style="margin: 0;">Just One Tablet!</p> <p style="margin: 0;">Prevents & Relieves Heartburn Due to Acid Indigestion</p> <h3 style="margin: 0;">50 Berries 'n' Cream Flavor Chewable Tablets</h3>	<p>Ask a doctor before use if you have • 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 • frequent chest pain • frequent vomiting, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. Stop use and ask a doctor if • your heartburn continues or worsens • you need to take this product for more than 14 days</p> <p>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.</p> <p>Directions • adults and children 12 years and over: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before eating/drinking at any time from 10 to 60 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor</p> <p>Dist. by: Johnson & Johnson • MERCK CONSUMER PHARMACEUTICALS CO., FORT WASHINGTON, PA 19028 USA ©Registered trademark of Merck & Co., Inc.</p>
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150% ACTUAL SIZE



Blister @ 100% Scale



Blister @ 200% Scale



Do not use if printed seal under bottle cap is open or torn.

Active Ingredient (in each tablet): Famotidine 20 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 food and beverages

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

Precautions: 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 if you have kidney disease, except under the advice of your doctor.

Other information: Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Famotidine is a tablet and children 12 years and over do not swallow tablet whole; chew completely to relieve symptoms, chew 1 tablet before swallowing to prevent symptoms, chew 1 tablet before swallowing at any time from 15 to 30 minutes before eating food or drinking beverages that cause heartburn. Do not use more than 2 tablets in 24 hours; children under 12 years: ask a doctor.

Excipients: Cellulose, croscarmellose sodium, hydroxypropyl methylcellulose, polyethylene glycol, polyethylene glycol 400, polyethylene glycol 600, polyethylene glycol 800, polyethylene glycol 1000, polyethylene glycol 1500, polyethylene glycol 2000, polyethylene glycol 3000, polyethylene glycol 4000, polyethylene glycol 6000, polyethylene glycol 8000, polyethylene glycol 10000, polyethylene glycol 15000, polyethylene glycol 20000, polyethylene glycol 30000, polyethylene glycol 40000, polyethylene glycol 60000, polyethylene glycol 80000, polyethylene glycol 100000, polyethylene glycol 150000, polyethylene glycol 200000, polyethylene glycol 300000, polyethylene glycol 400000, polyethylene glycol 600000, polyethylene glycol 800000, polyethylene glycol 1000000.

How to use: See the back of the bottle for full directions.

Keep out of reach of children.

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25 Chewable Tablets

Just One Tablet!

Prevents & Relieves Heartburn Due to Acid Indigestion

Cool Mint Flavor

25 Chewable Tablets

MAXIMUM STRENGTH

PEPCID AC

Famotidine Tablets 20 mg • Acid Reducer

EZ CHEWS

Prevents & Relieves Heartburn Due to Acid Indigestion

25 Chewable Tablets

Cool Mint Flavor

Just One Tablet!

Prevents & Relieves Heartburn Due to Acid Indigestion

Cool Mint Flavor

25 Chewable Tablets

7843334

150% ACTUAL SIZE

Do not use if printed seal under bottle cap is open or torn.

Active Ingredient (in each tablet): Famotidine 20 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 food and beverages

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

Precautions: 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 if you have kidney disease, except under the advice of your doctor.

Other information: Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Famotidine is a tablet and children 12 years and over do not swallow tablet whole; chew completely to relieve symptoms, chew 1 tablet before swallowing to prevent symptoms, chew 1 tablet before swallowing at any time from 15 to 30 minutes before eating food or drinking beverages that cause heartburn. Do not use more than 2 tablets in 24 hours; children under 12 years: ask a doctor.

Excipients: Cellulose, croscarmellose sodium, hydroxypropyl methylcellulose, polyethylene glycol, polyethylene glycol 400, polyethylene glycol 600, polyethylene glycol 800, polyethylene glycol 1000, polyethylene glycol 1500, polyethylene glycol 2000, polyethylene glycol 3000, polyethylene glycol 4000, polyethylene glycol 6000, polyethylene glycol 8000, polyethylene glycol 10000, polyethylene glycol 15000, polyethylene glycol 20000, polyethylene glycol 30000, polyethylene glycol 40000, polyethylene glycol 60000, polyethylene glycol 80000, polyethylene glycol 100000.

How to use: See the back of the bottle for full directions.

Keep out of reach of children.

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25 Chewable Tablets

Just One Tablet!

Prevents & Relieves Heartburn Due to Acid Indigestion

Cool Mint Flavor

25 Chewable Tablets

MAXIMUM STRENGTH

PEPCID AC

Famotidine Tablets 20 mg • Acid Reducer

EZ CHEWS

Prevents & Relieves Heartburn Due to Acid Indigestion

25 Chewable Tablets

Cool Mint Flavor

Just One Tablet!

Prevents & Relieves Heartburn Due to Acid Indigestion

Cool Mint Flavor

25 Chewable Tablets

7843334

Do not use if printed foil seal under bottle cap is open or torn.

Active ingredient (in each tablet): Famotidine 20 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 food and beverages

Warnings: • Allergy alert: Do not use if you are allergic to famotidine 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. • if you have kidney disease, except under the advice and supervision of a doctor with other acid reducers.

MAXIMUM STRENGTH NDC 10027-001-50

Pepcid[®] AC

Famotidine Tablets 20 mg • Acid Reducer

EZ CHEWS

Just One Tablet!

Prevents & Relieves Heartburn Due to Acid Indigestion

50 Cool Mint Flavor Chewable Tablets

Ask a doctor before use if you have • had heartburn over 3 months. This may be a sign of a more serious condition. • heartburn with light-headedness, sweating, or dizziness • chest pain or shoulder pain with shortness of breath, sweating, pain spreading to arms, neck or shoulder, or lightheadedness • frequent chest pain • frequent wheezing, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. 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: • do not chew tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before swallowing at any time • use 10 to 60 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: see a doctor.

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CONSUMER PHARMACEUTICALS CO., FORT WASHINGTON, PA 19024 USA
©Registered trademark of Merck & Co., Inc.

150% ACTUAL SIZE

Do not use if printed foil seal under bottle cap is open or torn.

Active ingredient (in each tablet): Famotidine 20 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 food and beverages

Warnings: • Allergy alert: Do not use if you are allergic to famotidine 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. • if you have kidney disease, except under the advice and supervision of a doctor with other acid reducers.

MAXIMUM STRENGTH NDC 10027-001-50

Pepcid[®] AC

Famotidine Tablets 20 mg • Acid Reducer

EZ CHEWS

Just One Tablet!

Prevents & Relieves Heartburn Due to Acid Indigestion

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Blister @ 100% Scale



Blister @ 200% Scale



<p>Do not use if printed foil seal under bottle cap is open or torn. Active ingredient (in each tablet) Famotidine 20 mg Purpose Acid reducer Use • 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 food and beverages Warning • Always take the rest of your acid reducer or other acid reducer • 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 if you have kidney disease, except under the advice and</p> <p>LOT: EXP: 7843542</p>	<p>MAXIMUM STRENGTH NDC 1837-385-25 Pepcid[®] AC Famotidine Tablets 20 mg • Acid Reducer EZ CHEWS Just One Tablet! Prevents & Relieves Heartburn Due to Acid Indigestion 25 Tropical Fruit Flavor Chewable Tablets</p>	<p>supervision of a doctor • with other acid reducers. Ask a doctor before use if you have • had heartburn over 2 months. This may be a sign of a more serious condition. • heartburn with nighttime awakenings, vomiting, or difficulty • chest pain or shoulder pain with shortness of breath, sweating, pain spreading to arms, neck or shoulder, or light-headedness • frequent chest pain • frequent retching, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. 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: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before swallowing at any time from 30 to 60 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor Dist. by: Johnson & Johnson • MERCK CONSUMER PHARMACEUTICALS CO., FORT WASHINGTON, PA 19084 USA ®Registered trademark of Merck & Co., Inc.</p>
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150% ACTUAL SIZE

<p>Do not use if printed foil seal under bottle cap is open or torn. Active ingredient (in each tablet) Famotidine 20 mg Purpose Acid reducer Use • 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 food and beverages Warning • Always take the rest of your acid reducer or other acid reducer • 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 if you have kidney disease, except under the advice and</p> <p>LOT: EXP: 7843542</p>	<p>MAXIMUM STRENGTH NDC 1837-385-25 Pepcid[®] AC Famotidine Tablets 20 mg • Acid Reducer EZ CHEWS Just One Tablet! Prevents & Relieves Heartburn Due to Acid Indigestion 25 Tropical Fruit Flavor Chewable Tablets</p>	<p>supervision of a doctor • with other acid reducers. Ask a doctor before use if you have • had heartburn over 2 months. This may be a sign of a more serious condition. • heartburn with nighttime awakenings, vomiting, or difficulty • chest pain or shoulder pain with shortness of breath, sweating, pain spreading to arms, neck or shoulder, or light-headedness • frequent chest pain • frequent retching, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. 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: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before swallowing at any time from 30 to 60 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor Dist. by: Johnson & Johnson • MERCK CONSUMER PHARMACEUTICALS CO., FORT WASHINGTON, PA 19084 USA ®Registered trademark of Merck & Co., Inc.</p>
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<p>Do not use if printed foil seal under bottle cap is open or torn. Active ingredient (in each tablet) Famotidine 20 mg</p> <p style="text-align: right;">Purpose Acid reducer</p> <p>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 food and beverages</p> <p>Warnings Allergy alert: Do not use if you are allergic to famotidine or other acid reducers</p> <p>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. • if you have kidney disease, except under the advice and supervision of a doctor • with other acid reducers</p> <p>LOT:</p> <p>EXP:</p> <p style="text-align: center;">7843543</p>	<p>MAXIMUM STRENGTH (NDC 0007-005-50)</p> <h1>Pepcid[®] AC</h1> <p>Famotidine Tablets 20 mg • Acid Reducer</p> <h2>EZ CHEWS</h2> <p>Just One Tablet! Prevents & Relieves Heartburn Due to Acid Indigestion</p> <p>50 Tropical Fruit Flavor Chewable Tablets</p>	<p>Ask a doctor before use if you have • 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 shoulder, or lightheadedness • frequent chest pain • frequent wheezing, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. Stop use and ask a doctor if • your heartburn continues or worsens • you need to take this product for more than 14 days</p> <p>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.</p> <p>Directions • adults and children 12 years and over: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before swallowing at any time from 10 to 60 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor</p> <p>Dist. by: Johanson-Johnson • MERCK CONSUMER PHARMACEUTICALS CO., FORT WASHINGTON, PA 19034 USA ©Registered trademark of Merck & Co., Inc.</p>
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150% ACTUAL SIZE

<p>Do not use if printed foil seal under bottle cap is open or torn. Active ingredient (in each tablet) Famotidine 20 mg</p> <p style="text-align: right;">Purpose Acid reducer</p> <p>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 food and beverages</p> <p>Warnings Allergy alert: Do not use if you are allergic to famotidine or other acid reducers</p> <p>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. • if you have kidney disease, except under the advice and supervision of a doctor • with other acid reducers</p> <p>LOT:</p> <p>EXP:</p> <p style="text-align: center;">7843543</p>	<p>MAXIMUM STRENGTH (NDC 0007-005-50)</p> <h1>Pepcid[®] AC</h1> <p>Famotidine Tablets 20 mg • Acid Reducer</p> <h2>EZ CHEWS</h2> <p>Just One Tablet! Prevents & Relieves Heartburn Due to Acid Indigestion</p> <p>50 Tropical Fruit Flavor Chewable Tablets</p>	<p>Ask a doctor before use if you have • 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 shoulder, or lightheadedness • frequent chest pain • frequent wheezing, particularly with heartburn • unexplained weight loss • nausea or vomiting • stomach pain. Stop use and ask a doctor if • your heartburn continues or worsens • you need to take this product for more than 14 days</p> <p>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.</p> <p>Directions • adults and children 12 years and over: • do not swallow tablet whole; chew completely • to relieve symptoms, chew 1 tablet before swallowing • to prevent symptoms, chew 1 tablet before swallowing at any time from 10 to 60 minutes before eating food or drinking beverages that cause heartburn • do not use more than 2 tablets in 24 hours • children under 12 years: ask a doctor</p> <p>Dist. by: Johanson-Johnson • MERCK CONSUMER PHARMACEUTICALS CO., FORT WASHINGTON, PA 19034 USA ©Registered trademark of Merck & Co., Inc.</p>
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**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
8/8/2007 11:08:07 AM
INTERDISCIPLINARY

Helen Cothran
8/8/2007 02:58:41 PM
INTERDISCIPLINARY

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-801/S-012

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	See Table C-1	
	Nonprescription Famotidine 20 mg Chewable Tablet	

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME Dennis M Erb, Ph D.	TITLE Vice President, Global Strategic Regulatory Development
FIRM/ORGANIZATION Merck & Co Inc	
SIGNATURE <i>Dennis M. Erb.</i>	DATE 1-23-07

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

Financial Disclosure Information

A. Introduction

In compliance with the U.S. Food and Drug Administration's regulation, *Financial Disclosure by Clinical Investigators*, published 02-Feb-1998 and revised 31-Dec-1998, the following sections detail the requested information concerning the financial interests of and compensation to investigators participating in the covered clinical study presented in this application.

Investigators meeting the definition of Clinical Investigator were requested to provide information related to their financial interests and/or arrangements (21 CFR 54.2) in Merck & Co., Inc. (hereinafter referred to as "Merck"). In compliance with the regulatory requirement for the Sponsor to demonstrate "due diligence" (21 CFR 54.4), multiple requests for this information were made, when possible, to clinical investigators who did not respond.

Data from the Clinical Study outlined in Table A-1 and A-2 are presented in this application.

Table A-1 provides a list of the covered clinical study as defined by 21 CFR 54.2(e) for the purpose of financial disclosure.

Table A-1 Summary of Covered Clinical Study				
Product/Protocol	Protocol Title	First Patient In	Last Patient Out	Financial Disclosure Information Cut-Off Date
0208-144	A Single-Dose, Open-Label, Three-Period Crossover Study to Assess the Bioequivalence of Famotidine 20 mg Film-Coated Tablets Compared to Famotidine 20 mg Meltaway with Water and Famotidine 20 mg Meltaway Without Water	18-Aug-2006	31-Aug-2006	10-Jan-2007

Table A-2 provides a list of each non-covered clinical study for the purpose of financial disclosure as defined by 21 CFR 54.2(e).

Table A-2 Summary of Non-Covered Clinical Study	
Product/Protocol	Protocol Title
Table A-2 is not applicable.	

Nonprescription Famotidine 20 mg Chewable Tablet
Financial Disclosure

Table A-3 details the total number of investigators in each of the categories that require reporting as defined in 21 CFR 54.2(a,b,c,f). As it is possible for an investigator to meet the definition for more than one category, the number of investigators in each sub-total may not add up to the total number of investigators.

Table A-3 Summary of Investigators by Category for the Covered Clinical Study			
Category	Description	Sub-Total	Total
B-1	Grand Total Number of All Investigators/Subinvestigators	N/A	4
C-1	Total Number of Investigators/Subinvestigators Certified Regarding the Absence of Financial Interests and Arrangements	N/A	4
C-2 *	Total Number of Investigators/Subinvestigators Not Certified	<ul style="list-style-type: none"> • Investigator deceased n= 0 • Investigator did not return requested information n= 0 • Investigator no longer at site n= 0 • Other n= 0 	0
D-1 **	Total Number of Investigators/Subinvestigators Who Hold Financial Interests or Arrangements Requiring Disclosure	<ul style="list-style-type: none"> • Compensation n= 0 • Equity Interest n= 0 • Proprietary or Financial Interest n= 0 • Significant Payments of Other Sorts n= 0 	0
* Refer to Table C-2 for investigator details as it is possible for an investigator to meet more than one sub-total description within Table A-3.			
** Refer to Table D-1 for investigator details as it is possible for an investigator to meet more than one sub-total description within Table A-3.			

B. Table of All Clinical Investigators/Subinvestigators

Table B-1 lists the names of all identified clinical investigators/subinvestigators by product, protocol and site number for the covered clinical study.

Table B-1 Table of All Clinical Investigators/Subinvestigators	
Product/Protocol/Site	Investigator/ Subinvestigator
0208-144-0001	(b) (4)

Nonprescription Famotidine 20 mg Chewable Tablet
Financial Disclosure

Table B-1 Table of All Clinical Investigators/Subinvestigators	
Product/Protocol/Site	Investigator/ Subinvestigator
	(b) (4)

Table B-2 lists the names of all identified clinical investigators/subinvestigators by product, protocol and site number for the covered clinical study who have reported either themselves, a spouse and/or each dependent child as a Merck employee.

Table B-2 Table of Merck Employees		
Product/Protocol/Site	Investigator/ Subinvestigator	Merck Employee
Table B-2 is not applicable.		

C. Form FDA 3454 – Certification: Financial Interests and Arrangements of Clinical Investigators

Certification for the financial interests and arrangements of clinical investigators/subinvestigators participating in the covered clinical study is attached; this information is reflective of the requirements outlined in 21 CFR 54.4(a)(1).

Table C-1 lists the names of all identified clinical investigators/subinvestigators by product, protocol and site number for the covered clinical study who have met the certification criteria regarding an absence of financial interests and arrangements as defined in 21 CFR 54.2.

Table C-1 Table of All Clinical Investigators/Subinvestigators Certified Regarding the Absence of Financial Interests and Arrangements	
Product/Protocol/Site	Investigator/ Subinvestigator
0208-144-0001	(b) (4)

Nonprescription Famotidine 20 mg Chewable Tablet
Financial Disclosure

Table C-2 lists the names of all identified clinical investigators/subinvestigators by product, protocol and site number for the covered clinical study who did not provide the requested information by the cut-off date and includes the reason(s) the investigator could not be certified. In compliance with the regulatory requirement for the Sponsor to demonstrate "due diligence" (21 CFR 54.4), multiple requests for this information were made, when possible, to investigators who did not respond.

Table C-2 Table of All Clinical Investigators/Subinvestigators Not Certified		
Product/Protocol/Site	Investigator/ Subinvestigator	Reason
Table C-2 is not applicable.		

D. Form FDA 3455 – Disclosure: Financial Interests and Arrangements of Clinical Investigators

Disclosure of the financial interests of investigator/subinvestigators participating in the covered clinical study is attached; this information is reflective of 21 CFR 54.4(a)(3).

Table D-1 lists the names of all identified clinical investigators/subinvestigators by product, protocol and site number for the covered clinical study who have met the disclosure criteria regarding financial interests and arrangements as defined in 21 CFR 54.2(a,b,c,f).

Bias has been minimized, when appropriate, through study design, e.g., double- or triple-blind, placebo-controlled, multicenter study sites, etc.

Table D-1 Table of All Clinical Investigators/Subinvestigators Who Hold Financial Interests or Arrangements Requiring Disclosure		
Product/Protocol/Site	Investigator/ Subinvestigator	Financial Interests or Arrangements
Table D-1 is not applicable.		

ACTION PACKAGE CHECKLIST

Application Information		
BLA # NDA # 20-801	BLA STN# NDA Supplement # S-012	If NDA, Efficacy Supplement Type
Proprietary Name: Pepcid AC Established Name: 20 mg famotidine Dosage Form: Chewable tablets		Applicant: Merck, Inc
RPM: Keith Olin	Division: DNCE	Phone # 301-796-0962
<p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>Efficacy Supplement: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>	<p>505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct.</p> <p><input type="checkbox"/> Confirmed <input type="checkbox"/> Corrected</p> <p>Date:</p>	
❖ User Fee Goal Date		
❖ Action Goal Date (if different)		
❖ Actions		
• Proposed action	<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR	
• Previous actions (<i>specify type and date for each action taken</i>)	<input type="checkbox"/> None	
❖ Advertising (<i>approvals only</i>) Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed (<i>indicate dates of reviews</i>)		<input type="checkbox"/> Requested in AP letter <input type="checkbox"/> Received and reviewed

❖ Application Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): NDAs, BLAs and Supplements: <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2 <input type="checkbox"/> Orphan drug designation NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies NDAs and NDA Supplements: <input checked="" type="checkbox"/> OTC drug Other: Other comments:	
❖ Application Integrity Policy (AIP)	
<ul style="list-style-type: none"> • Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> • Exception for review (<i>file Center Director's memo in Administrative Documents section</i>) • OC clearance for approval (<i>file communication in Administrative Documents section</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not an AP action
❖ Public communications (approvals only)	
<ul style="list-style-type: none"> • Office of Executive Programs (OEP) liaison has been notified of action 	<input type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> • Press Office notified of action 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

<p>notice of certification?</p> <p>(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).</p> <p><i>If "Yes," skip to question (4) below. If "No," continue with question (2).</i></p> <p>(2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?</p> <p><i>If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "No," continue with question (3).</i></p> <p>(3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).</p> <p><i>If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.</i></p> <p>(4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?</p> <p><i>If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "No," continue with question (5).</i></p> <p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
--	--

<p>within the 45-day period).</p> <p><i>If “No,” there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If “Yes,” a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.</i></p>	
<i>Summary Reviews</i>	
<p>❖ Summary Reviews (e.g., Office Director, Division Director) (<i>indicate date for each review</i>)</p>	
<p>❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (<i>indicate date</i>)</p>	
<i>Labeling</i>	
<p>❖ Package Insert</p>	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	<p>March 23, 2007</p>
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	<p>March 23, 2007</p>
<p>❖ Patient Package Insert</p>	
<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
<p>❖ Medication Guide</p>	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling) 	
<p>❖ Labels (full color carton and immediate-container labels)</p>	
<ul style="list-style-type: none"> • Most-recent division-proposed labels (only if generated after latest applicant submission) 	<p>March 23, 2007</p>
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	
<p>❖ Labeling reviews and minutes of any labeling meetings (<i>indicate dates of reviews and meetings</i>)</p>	<p> <input type="checkbox"/> DMETS <input type="checkbox"/> DSRCS <input type="checkbox"/> DDMAC <input type="checkbox"/> SEALD <input checked="" type="checkbox"/> Other reviews August 8, 2007 <input type="checkbox"/> Memos of Mtgs </p>

Administrative Reviews/Approvals	
❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) (<i>indicate date of each review</i>)	December 14, 2007
❖ NDA and NDA supplement approvals only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/> Included
❖ AIP-related documents <ul style="list-style-type: none"> • Center Director's Exception for Review memo • If AP: OC clearance for approval 	
❖ Pediatric Page (all actions)	<input checked="" type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent. (<i>Include certification.</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Postmarketing Commitment Studies <ul style="list-style-type: none"> • Outgoing Agency request for post-marketing commitments (<i>if located elsewhere in package, state where located</i>) • Incoming submission documenting commitment 	<input type="checkbox"/> None
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	
❖ Internal memoranda, telecons, email, etc.	
❖ Minutes of Meetings <ul style="list-style-type: none"> • Pre-Approval Safety Conference (<i>indicate date; approvals only</i>) • Pre-NDA/BLA meeting (<i>indicate date</i>) • EOP2 meeting (<i>indicate date</i>) • Other (e.g., EOP2a, CMC pilot programs) 	<input type="checkbox"/> No mtg <input type="checkbox"/> No mtg May 22, 2006
❖ Advisory Committee Meeting <ul style="list-style-type: none"> • Date of Meeting • 48-hour alert or minutes, if available 	<input type="checkbox"/> No AC meeting
❖ <u>Federal Register</u> Notices, DESI documents, NAS/NRC reports (if applicable)	
CMC/Parenteral (p.o. or i.v.)	
❖ CMC/Product review(s) (<i>indicate date for each review</i>)	October 25, 2007
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer (<i>indicate date for each review</i>)	<input type="checkbox"/> None
❖ BLAs: Product subject to lot release (APs only)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Environmental Assessment (check one) (original and supplemental applications) <ul style="list-style-type: none"> • <input type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>) • <input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>) • <input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>) 	
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) (<i>indicate date of each review</i>)	<input type="checkbox"/> Not a parenteral product
❖ Facilities Review/Inspection <ul style="list-style-type: none"> • NDAs: Facilities inspections (include EER printout) 	Date completed: <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation

❖ BLAs: Facility-Related Documents <ul style="list-style-type: none"> • Facility review (<i>indicate date(s)</i>) • Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>) 	<input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold
❖ NDAs: Methods Validation	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed
Nonclinical Reviews	
❖ Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	
❖ Nonclinical inspection review Summary (DSI)	<input type="checkbox"/> None requested
Additional Reviews	
❖ Clinical review(s) (<i>indicate date for each review</i>)	
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	
❖ Clinical consult reviews from other review disciplines/divisions/Centers (<i>indicate date of each review</i>)	<input type="checkbox"/> None
❖ Microbiology (efficacy) reviews(s) (<i>indicate date of each review</i>)	<input type="checkbox"/> Not needed
❖ Safety Update review(s) (<i>indicate location/date if incorporated into another review</i>)	
❖ Risk Management Plan review(s) (including those by OSE) (<i>indicate location/date if incorporated into another review</i>)	
❖ Controlled Substance Staff review(s) and recommendation for scheduling (<i>indicate date of each review</i>)	<input type="checkbox"/> Not needed
❖ DSI Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input type="checkbox"/> None requested
• Clinical Studies	
• Bioequivalence Studies	
• Clin Pharm Studies	
❖ Statistical Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
❖ Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None

Sept 24, 2007

Appendix A to Action Package Checklist

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

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

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

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

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

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

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

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

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

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

/s/

Geraldine Smith
12/14/2007 05:02:58 PM
for Keith Olin

Paulette Midgette, MS
Manager, Regulatory Liaison
Worldwide OTC Regulatory Affairs

Merck & Co., Inc.
UN-D129
PO Box 4
West Point, PA 19486
Tel 267 305 8731
Fax 267 305 8907
paulette_midgette@merck.com



May 19, 2008

Andrea Leonard-Segal, M.D., Director
Food and Drug Administration
Center of Drug Evaluation and Research
Office of Nonprescription Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

Dear Dr. Leonard-Segal:

**NDA 20-801: PEPCID™ AC Chewable Tablets
(nonprescription famotidine)**

TIME SENSITIVE PATENT INFORMATION

Reference is made to the supplemental/New Drug Application cited above for PEPCID™ AC Chewable Tablets submitted as an electronic archive on March 23, 2007 and to an approval letter dated December 17, 2007 regarding this application. Reference is also made to an April 22, 2008 Submission of Time-Sensitive Patent Information to the NDA and FDA Orange Book Staff. Final reference is made to a telephone communication between Ms. Paulette Midgette of MRL and Ms. Maryann Holovac of the FDA, regarding Patent 114 expiration date discrepancy.

As indicated on the attached Form 356h and in accordance with 21 CFR §314.53(d), this submission provides for updates to the Patent Section for nonprescription famotidine 20 mg. Specifically, this submission includes an updated FDA Form 3542 indicating a change in the patent expiration date of the 10 mg Chewable Tablet.

This submission is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs*. This submission is being transmitted through the FDA's electronic submission gateway.

A list of reviewers from the Office of Nonprescription Products, who should be provided access to this electronic submission on their desktops, may be obtained from Geri Smith, Regulatory Project Manager, Office of Nonprescription Products.

Andrea Leonard-Segal, M.D., Director
NDA 20-801: PEPCID™ AC Chewable Tablets
(nonprescription famotidine)
Page 2

We consider the filing of this submission to be a confidential matter and request that the Food and Drug Administration not make its content, or any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this submission should be directed to Ms. Paulette Midgette (267-305-8731) or in my absence, to Edwin L. Hemwall, Ph.D. (267-305- 8406).

Sincerely,



Paulette Midgette, M.S.
Manager, Regulatory Affairs
Johnson & Johnson • Merck
Consumer Pharmaceuticals Co.

Desk Copy: Maryann Holovac (cover letter and patent)
Center for Drug Evaluation and Research
Orange Book Staff
Office of Generic Drugs
HFD-610
7500 Standish Place
Rockville, MD 20855

Nonprescription Famotidine Chewable Tablets 20 mg
1.9.1 Request for Waiver of Pediatric Studies

Johnson & Johnson • Merck Consumer Pharmaceuticals Co. requests a waiver of pediatric studies for Nonprescription Famotidine 20 mg chewable tablets, according to the final Pediatric Rule (21 CFR 314.55(a) and 601.27(a)).

Approved labeling for PEPCID™ COMPLETE, an OTC product containing famotidine 10 mg and antacid, allows for the treatment of individuals above 12 years of age. The rationale for this age limit is that children below the age of 12 years who exhibit symptoms consistent with the approved indications for PEPCID™ COMPLETE should only use it, or famotidine-containing prescription products, under the direction of a physician, and a pediatric waiver was granted by FDA for this product. We believe that the same rationale and approach is appropriate for a 20-mg OTC famotidine chewable product.

The proposed labeling for Nonprescription Famotidine 20 mg chewable tablets contains a direction for use by “adults and children 12 years and over”. and “children under 12 years: ask a doctor”.

(b) (4)

(b) (4)

REQUEST FOR WAIVER OF PEDIATRIC STUDIES

IND/NDA/BLA number (as applicable): **NDA 20-801: Pepcid™ AC Chewable Tablets**
Nonprescription Famotidine 20 mg

Sponsor: Johnson & Johnson • Merck Consumer Pharmaceuticals Co.

Indications(s): Treatment or prevention of heartburn associated with acid indigestion and sour stomach

1. What age ranges are included in your waiver request? Less than 12 years of age
2. Reasons for waiving pediatric studies:
 - (a) No meaningful therapeutic benefit over existing treatments **and** is unlikely to be used in a substantial number of pediatric patients.
 - (b) Studies are impossible or highly impractical because the number of patients is so small or geographically dispersed
 - (c) The product would be ineffective or unsafe in all pediatric age groups
 - (d) Attempts to develop a pediatric formulation for a specific age group have failed
 - (e) Disease-specific waiver indicated for the treatment of the condition in adults (please check)

Alzheimer's disease
 Prostate Cancer
 Renal cell cancer
 Hairy cell cancer
 Osteoarthritis
 Uterine cancer
 Endometrial cancer
 Parkinson's disease
 Arteriosclerosis
 Infertility

Age-related macular degeneration
 Breast cancer
 Non-germ cell ovarian cancer
 Pancreatic cancer, colorectal cancer
 Squamous cell cancers of the oropharynx
 Basal cell and squamous cell cancer
 Small cell and non-small cell lung cancer
 Amyotrophic lateral sclerosis
 Symptoms of menopause
 Other (please state and justify)

3. Justification for waiver (not necessary if category 2(e) is checked):

Proposed labeling for this over-the-counter (OTC) product allows for the treatment of individuals 12 years of age or over. Children below the age of 12 years who exhibit symptoms consistent with the proposed indications should only use this, or famotidine-containing prescription products, under the direction of a physician. Therefore, pediatric studies are not appropriate for this OTC product, (b) (4)

Item 16 - Debarment Certification

As required by §306(k)(1) of 21 U.S.C. 335a(k)(1), we hereby certify that, in connection with this application, Merck & Co., Inc. did not and will not use in any capacity the services of any person debarred under subsections 306(a) or (b) of the Act.

Brenda A. McGuire

Brenda A. McGuire, M.S., R.N.
Associate Director
Regulatory Affairs

March 23, 2007

Date

Brenda A. McGuire, M.S., R.N.
Associate Director
Worldwide OTC Regulatory Affairs

Merck & Co., Inc.
UN-D129
P.O. Box 4
West Point PA 19486
Tel 484 344 7235
Fax 484 344 3682
brenda_mcguire@merck.com

March 23, 2007



Andrea Leonard-Segal, M.D., Director
Food and Administration
Center for Drug Evaluation and Research
Division of Nonprescription Clinical Evaluation
5901-B Ammendale Road
Beltsville, MD 20705-1266

Dear Dr. Leonard-Segal:

**NDA 20-801: PEPCID™ AC Chewable Tablets
(nonprescription famotidine)**

**Prior Approval Supplement
(nonprescription famotidine 20 mg)**

Reference is made to the New Drug Application noted above, and to a meeting held on May 22, 2006 between Merck Research Laboratories (MRL), a division of Merck & Co., Inc., Johnson & Johnson • Merck Consumer Pharmaceuticals Co. (JJCPC), and representatives of the FDA Divisions of Nonprescription Clinical Evaluation, Nonprescription Regulation Development, Pharmaceutical Evaluation-III, and Office of New Drug Quality Assessment, to discuss the requirements of a development program that would support approval of a famotidine 20 mg chewable tablet. Additional reference is made to a telephone conversation between Dr. Edwin Hemwall (JJCPC) and Dr. Charles Ganley and Dr. Andrea Leonard-Segal (FDA) on February 21, 2007, during which the plans and timing for this submission were discussed.

The trade name of "Maximum Strength PEPCID™ AC EZ Chews" is being proposed for this new product. This new formulation provides a chewable tablet with an improved taste and mouth feel at a 20 mg dose, and will replace the currently approved PEPCID™ AC 10 mg Chewable Tablet product in the marketplace. Manufacture of the current 10-mg PEPCID™ AC Chewable Tablet formulation has been discontinued.

As indicated on the attached Form FDA 356h, this supplemental application provides for changes in the Labeling, Chemistry, Manufacturing and Controls and Human Pharmacology & Bioavailability/Bioequivalence Sections of the approved New Drug Application for PEPCID™ AC Chewable Tablets in support of a 20-mg chewable product. The manufacturing sites, McNeil Consumer Healthcare, Las Piedras, PR and Johnson & Johnson • Merck Consumer Pharmaceuticals, Lancaster, PA, and the packaging sites, Johnson & Johnson • Merck Consumer Pharmaceuticals, Lancaster, PA and ^{(b) (4)} are prepared for a Pre-Approval Inspection (PAI) in connection with this supplemental NDA.

Consistent with the FDA/Sponsor discussions that took place on February 21st as well as FDA initiatives to make the NDA review process more efficient, the Sponsor requests that comments on the labeling contained in this submission be provided before the Action Goal date, so any issues can be resolved prior to the issuance of the Action letter.

Background

At a FDA/Sponsor teleconference meeting held on May 22, 2006, JJMCPC provided the Agency with a plan to develop a new chewable formulation of the approved PEPCID™ AC Chewable Tablets (10 mg). This new product, a 20-mg chewable tablet, has an improved taste and mouth feel and will replace the current 10-mg chewable tablet in the marketplace. A nonprescription famotidine 20 mg product is currently available only as a film-coated tablet (NDA 20-325, Maximum™ Strength PEPCID AC 20 mg FCT).

At the May 22nd meeting FDA concurred with the Sponsor's proposal to file this application as a supplement to NDA 20-801, stipulating that the new formulation must be a chewable dosage form. Also agreed upon were the study design and treatment arms for a bioequivalence study. Accordingly, a bioequivalence study (Study 144) has been conducted which compared the new formulation to the reference product (famotidine 20 mg FCT), with and without water. The results of this study demonstrate that the new chewable formulation is bioequivalent to the FCT reference standard when taken both with and without water. These results are summarized in the Clinical Overview section as well as the Clinical Study Report included in this submission.

The FDA has advised that any potential for a food interaction for the new formulation be addressed in the application. JJMCPC believes that sufficient data exist from previous famotidine PK and Safety and Efficacy studies (when the product was taken after or just before meals) to adequately understand the clinical importance of any potential interaction of famotidine in this formulation with food. This prior experience and knowledge supports the Sponsor's position that no food interaction studies are necessary. A more complete explanation of this position is provided in the Clinical Overview section.

Labeling

The proposed product label for Maximum Strength PEPCID™ AC EZ Chews has been created by combining the currently approved PEPCID™ AC Chewable Tablets (10 mg) Drug Facts label with selected elements of the Maximum Strength PEPCID™ AC FCT Drug Facts label added that are relevant to a 20-mg strength famotidine product.

The additional label statements include:

- In the **Do not use** section, bullet stating "*if you have kidney disease, except under the advice and supervision of a doctor*".
- In the **Directions** section, the timeframe associated with a 20-mg product being used for heartburn prevention has been applied: "*to prevent symptoms, chew 1 tablet before swallowing at any time from 10 to 60 minutes before eating food or drinking beverages that cause heartburn*".

Other modifications made to the current PEPCID™ AC Chewable Tablets package and label include:

- The text and artwork on the principal display panel are consistent with currently approved packaging for the entire PEPCID product line with the exception of the phrase “Can take without water”. This phrase was added to the front panel to inform consumers at the point of purchase of this special feature of the product, and is substantiated by the results of the bioequivalence study 144.
- Based on stability testing, the storage temperature range has been established at 20°-25°C (68°-77°F). Information supporting this statement is included in the CMC section of this application.
- Three flavors of the new product will be offered (Berries ‘n’ Cream, Cool Mint, and Tropical Fruit) and each has minor flavor and color variations included in the list of inactive ingredients.

With this submission are the following items:

I. Carton label

- | | |
|------------------------------|---|
| a. 8-ct Carton (Berries) | (proposed-trade-carton-msssoftchewb-8-pouchcart.pdf) |
| b. 8-ct Carton (Mint) | (proposed-trade-carton-msssoftchewm-8-pouchcart.pdf) |
| c. 8-ct Carton (Trop Fruit) | (proposed-trade-carton-msssoftchewtf-8-pouchcart.pdf) |
| d. 25-ct Carton (Berries) | (proposed-trade-carton-msssoftchewb-25-botcart.pdf) |
| e. 25-ct Carton (Mint) | (proposed-trade-carton-msssoftchewm-25-botcart.pdf) |
| f. 25-ct Carton (Trop Fruit) | (proposed-trade-carton-msssoftchewtf-25-botcart.pdf) |
| g. 50-ct Carton (Berries) | (proposed-trade-carton-msssoftchewb-50-botcart.pdf) |
| h. 50-ct Carton (Mint) | (proposed-trade-carton-msssoftchewm-50-botcart.pdf) |
| i. 50-ct Carton (Trop Fruit) | (proposed-trade-carton-msssoftchewtf-50-botcart.pdf) |

II. Container label

- | | |
|------------------------------------|---|
| a. 25-ct Bottle Label (Berries) | (proposed-trade-container-msssoftchewb-25-botlab.pdf) |
| b. 25-ct Bottle Label (Mint) | (proposed-trade-container-msssoftchewm-25-botlab.pdf) |
| c. 25-ct Bottle Label (Trop Fruit) | (proposed-trade-container-msssoftchewtf-25-botlab.pdf) |
| d. 50-ct Bottle Label (Berries) | (proposed-trade-container-msssoftchewb-50-botlab.pdf) |
| e. 50-ct Bottle Label (Mint) | (proposed-trade-container-msssoftchewm-50-botlab.pdf) |
| f. 50-ct Bottle Label (Trop Fruit) | (proposed-trade-container-msssoftchewtf-50-botlab.pdf) |
| g. 1-ct Sample Pouch (Berries) | (proposed-trade-container-msssoftchewb-1-samplpouch.pdf) |
| h. 1-ct Sample Pouch (Mint) | (proposed-trade-container-msssoftchewm-1-samplpouch.pdf) |
| i. 50x1 Dispensit (Berries) | (proposed-trade-container-msssoftchewb-50-dispensit.pdf) |
| j. 50x1 Dispensit (Mint) | (proposed-trade-container-msssoftchewm-50-dispensit.pdf) |
| k. 1-ct Trade Pouch (Berries) | (proposed-trade-container-msssoftchewb-1-tradepouch.pdf) |
| l. 1-ct Trade Pouch (Mint) | (proposed-trade-container-msssoftchewm-1-tradepouch.pdf) |
| m. 1-ct Trade Pouch (Trop Fruit) | (proposed-trade-container-msssoftchewtf-1-tradepouch.pdf) |

In accordance with the Food and Drug Administration Modernization Act of 1997 (FDAMA), as indicated in the attached FDA Form 3397, no user fee is required for this supplemental application.

Andrea Leonard-Segal, M.D., Director
NDA 20-801: PEPCID™ AC Chewable Tablets
Page 4

This supplemental application is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs. This submission is being transmitted through the FDA's electronic submission gateway.

A list of reviewers from the Office of Nonprescription Products who should be provided access to this electronic submission on their desktops may be obtained from Michelle Williamson, Regulatory Project Manager, Office of Nonprescription Products.

We consider the filing of this supplemental New Drug Application to be a confidential matter, and request that the Food and Drug Administration not make its content, or any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this supplemental application should be directed to Brenda A. McGuire, M.S., R.N. (484-344-7235) or, in my absence, Edwin L. Hemwall, Ph.D. (484-344-2306).

Sincerely,



Brenda A. McGuire, M.S., R.N.
Associate Director
Worldwide OTC Regulatory Affairs

Desk Copies: Michelle Williamson (cover letter)
Regulatory Project Manager
Division of Nonprescription Products

Maryann Holovac (cover letter and patent)
Orange Book Staff
Office of Generic Drugs
HFD-610, Room 134
7500 Standish Place
Rockville, MD 20855-2773



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 20-801/S-012

Merck & Co, Inc.
Attention: Brenda McGuire, M.S., R.N.
Associate Director
Worldwide OTC Regulatory Affairs
Sumneytown Pike
P.O. Box 4, UN-D129
West Point, PA 19486

Dear Ms. McGuire:

Please refer to your March 23, 2007 supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pepcid AC Chewable (10mg famotidine) tablet.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on May 22, 2007 in accordance with 21 CFR 314.101(a).

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

If you have any questions, call Keith Olin, Regulatory Project Manager, at (301) 796-0962.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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this page is the manifestation of the electronic signature.**

/s/

Leah Christl

6/1/2007 04:01:43 PM



NDA 20-801/S-012

PRIOR APPROVAL SUPPLEMENT

Merck & Co., Inc.
Attention: Brenda McGuire, M.S., R.N.
Associate Director
Worldwide OTC Regulatory Affairs
Sumneytown Pike
P.O. Box 4, UN-D129
West point, PA 19486

Dear Ms. McGuire:

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:	Pepcid AC Chewable (10 mg famotidine) tablets
NDA Number:	20-801
Supplement number:	012
Review Priority Classification:	Standard (S)
Date of supplement:	March 23, 2007
Date of receipt:	March 23, 2007

This supplemental application proposes a new dosing regimen with a new 20 mg strength chewable tablet and a new softer chewable tablet formulation. The supplement is also proposing a new tradename "Maximum Strength PEPCID AC EZ Chews".

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 May 22, 2007, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be January 23, 2008.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirement. We are waiving the requirement for pediatric studies for this application.

NDA 21-801/S-012

Page 2

Please cite the application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Nonprescription Clinical Evaluation
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any question, call Keith Olin, Regulatory Project Manager, at (301) 796-0962.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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this page is the manifestation of the electronic signature.**

/s/

Leah Christl

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