CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: 020951

Trade Name: TAGAMET HB 200 SUSPENSION

Generic Name: CIMETIDINE

Sponsor: SMITH KLINE BEECHAM CONSUMER HEALTHCARE

Approval Date: 07/09/99

INDICATION(s): FOR THE RELIEF OF HEARTBURN ASSOCIATED WITH ACID INDIGESTION AND SOUR STOMACH AND FOR PREVENTION OF HEARTBURN ASSOCIATED WITH ACID INDIGESTION AND SOUR STOMACH BROUGHT ON BY EATING OR DRINKING CERTAIN FOOD AND BEVERAGES.

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Application Number: 020951

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-951

SmithKline Beecham Consumer Healthcare
Attention: Robert Harris
Senior Regulatory Affairs Specialist
1500 Littleton Road
Parsippany, NY 07054-3884

JUL 9 1999

Dear Mr. Harris:

Please refer to your new drug application (NDA) dated December 29, 1997, received December 30, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nonprescription Tagamet HB 200® (cimetidine) Suspension.

We acknowledge receipt of your submissions dated January 8, April 1 and 30, May 27, and June 17, 1999. Your submission of January 8, 1999 constituted a complete response to our December 17, 1998 action letter.

This new drug application provides for the use of Nonprescription Tagamet HB 200 (cimetidine) Suspension for relief of heartburn associated with acid indigestion and sour stomach and for prevention of heartburn associated with acid indigestion and sour stomach brought on by eating or drinking certain food and beverages.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted labeling of May 27, 1999, with the revisions listed below. Accordingly, the application is approved effective on the date of this letter.

As agreed in your telephone conversations with Ms. Kacuba on July 6 and 8, 1999, the revisions are as follows:

1. 2 FLUID OZ. TRIAL AND 2 FLUID OZ. SAMPLE BOTTLE LABELS

   a. Revise the labels to meet all the requirements of 21 CFR 201.66 for the standard labeling format.

   b. To conserve space on these labels, the "Clinically Proven" section containing the bar graphs and text may be deleted.

2. ALL BOTTLE LABELS

The following revisions must be made to the 2 fluid oz. trial and sample bottle labels and the 12 fluid oz. retail bottle label:

a. Revise the visible panel of the folded back label to increase the prominence of the directions, "OPEN HERE" or "OPEN HERE FOR DRUG FACTS INFORMATION" to assist the consumer in locating the Drug Facts information.

b. ***Warnings***: For consistency with 21 CFR 201.66:

i. Capitalize the first letter of the **Allergy alert** warning to read: "**Allergy alert**: Do not use if you are allergic to cimetidine or other acid reducers".

ii. To emphasize that this product is not intended for children under 12 years of age, the following bulleted, bolded statement must appear under the "**Warnings**", "**Do not use**" section:

"■ **in children under 12 years (see Directions)**"

This warning must appear in the ***Warnings*** section, in addition to the ***Directions*** section.

iii. Revise the text under the subheading "**Ask a doctor or pharmacist before use if you are taking,**" to read:

"■ **theophylline (oral asthma medicine)**
■ **warfarin (blood thinning medicine)**
■ **phenytoin (seizure medicine)**

If you are not sure you are taking one of these medicines, talk to your doctor or pharmacist."

iv. Left align the "**Keep out of reach of children**" warning.

c. ***Directions***: For consistency with other OTC drug product labels:

i. In the second and third bullets, revise the word "older" to "over" to read:

"■ adults and children 12 years and over:..."

ii. Revise the fourth bullet to read:

"■ do not take more than 4 teaspoons twice in 24 hours"

iii. To save label space and to promote safe use of the product by emphasizing (bolding) that the consumer should not use the product for children, revise the fifth bullet to read:

"■ children under 12 years: **not for use in children under 12. The safety and effectiveness for use in children under 12 has not been proven.**"

iv. For consistency with 21 CFR 201.66, revise the format so that the bulleted statements are aligned as reflected below:

"■ shake well
■ adults and children 12 years and over:
  ■ to **relieve** symptoms, take 4 teaspoons (20mL) in premeasured dose cup provided, with a glass of water
  ■ to **prevent** symptoms, take 4 teaspoons (20mL) in premeasured dose cup provided, with a glass of water **right before or any time up to 30 minutes before** eating food or drinking beverages that cause heartburn
  ■ do not take more than 4 teaspoons twice in 24 hours
■ children under 12 years: **not for use in children under 12. The safety and effectiveness for use in children under 12 has not been proven.**

d. ***Other information:*** For consistency with other OTC drug product labels, revise the storage statement from:

"■ store between 20° - 30°C (68° - 86°F)"

to:

"■ store at 20 - 30°C (68 - 86°F)"

e. ***Questions or comments?*** For consistency with 21 CFR 201.66, remove upper case letters from the phrase "Call Toll-Free" to read:

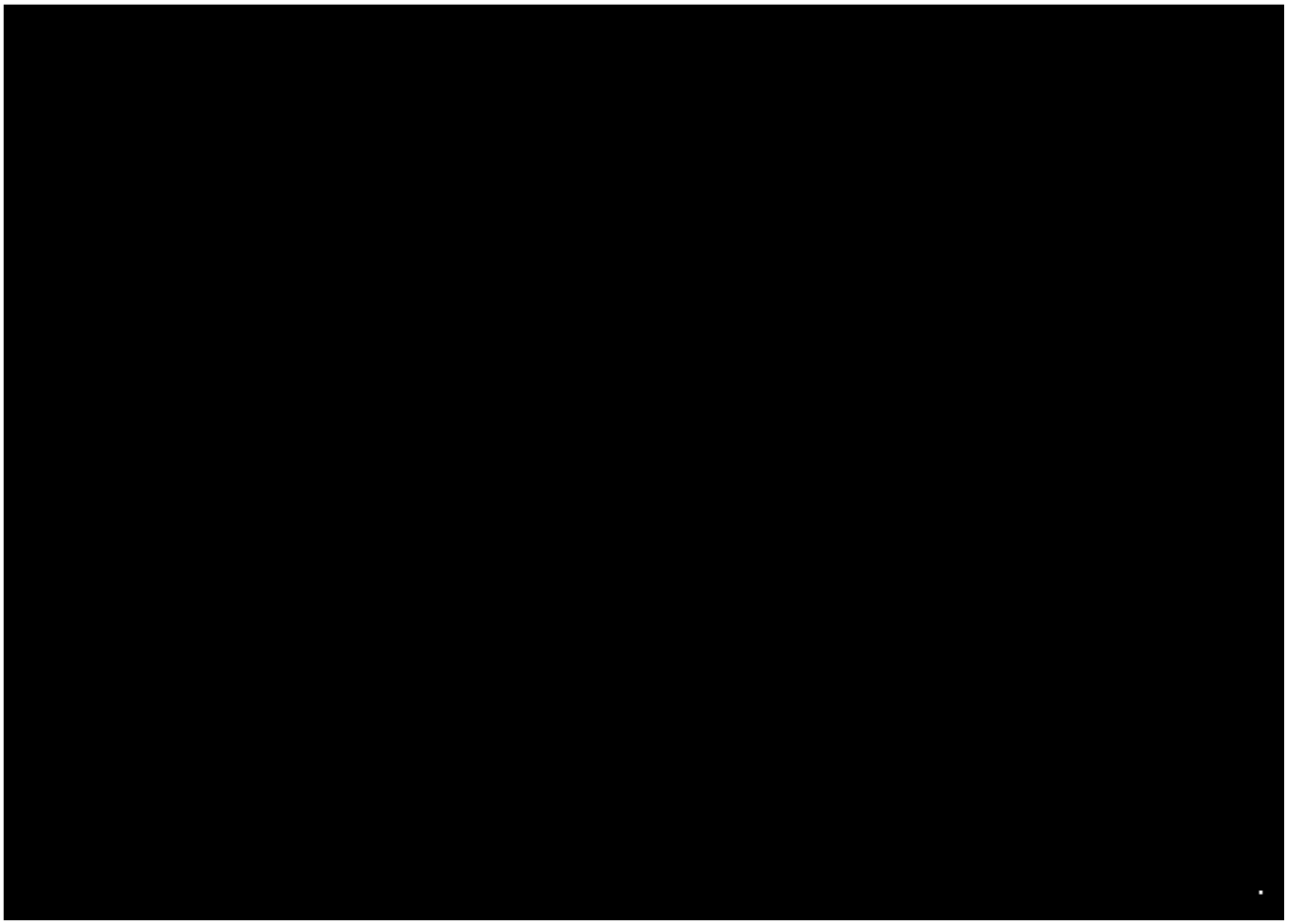
"call toll-free..."

In addition to the above, revise the words "for relief of" and "for prevention of" to "relieves" and "prevents," respectively, in the ***Uses*** section.

These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as requested, in the product's final printed labeling (FPL) may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-951." Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of the labeling may be required.



[redacted]

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Finally, please submit four copies of the introductory promotional mateials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Gastrointestinal and Coagulation Drug Products, one to the Division of Over-the-Counter Drug Products, and two copies of both the promotional materials and the labeling directly to:

Division of Drug Marketing, Advertising and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please submit one market package of the drug product when it is available.

Be advised that, as of April 1, 1999, 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 (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27). We are deferring submission of your pediatric studies until December 2, 2001. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov.cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" in addition to your plans for pediatric drug development described above. If you do not submit a Proposed Pediatric Study Request within 120 days from the date of this letter, we will presume that you are not interested in obtaining pediatric exclusivity [NOTE: You should still submit a pediatric drug development plan.] and will notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

In line with Center for Drug Evaluation and Research policy, oversight of this application is being transferred to the Division of Over-the-Counter Drug Products. If you have any questions, please contact Albert Rothschild at (301) 827-2222.

Sincerely,

[redacted]
/S/

Charles Ganley, M.D.
Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

[redacted]
/S/

Lilia Talarico, M.D.
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