CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-586/S-004

ADMINISTRATIVE DOCUMENTS AND CORRESPONDENCE

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: 04/09/01	**DUE DATE:** 04/23/01	**OPDRA CONSULT #:** 01-0081

TO: Renata Albrecht, M.D.
Director, Division of Special Pathogen and Immunologic Drug Products
(HFD-590)

THROUGH: Leo Chan
Project Manager
(HFD-590)

PRODUCT NAME:	**DISTRIBUTOR:** Meretek Diagnostics, Inc.
Pranactin-Citric (^{13}C-Urea solution) 75 mg A drug component of **BreathTek UBT**. **NDA #: 20-586 SE-004**	

SAFETY EVALUATOR: Hye-Joo Kim, Pharm.D.

SUMMARY: In response to a consult from the Division of Special Pathogen and Immunologic Drug products, OPDRA conducted a review of the proposed proprietary name, Pranactin-Citric.

OPDRA RECOMMENDATION: OPDRA does not recommend the use of the proprietary name, Pranactin-Citric. See review for details.

APPEARS THIS WAY
ON ORIGINAL

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Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm. 15B-03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: **April 17, 2001**

NDA NUMBER: **20-586 SE-004**

NAME OF DRUG: **Pranactin-Citric**
(^{13}C-Urea solution) 75 mg
A drug component of **BreathTek UBT**

NDA HOLDER: **Meretek Inc.**

I. INTRODUCTION

This consult was written in response to a request from the Division of Special Pathogen and Immunologic Drug products (HFD-590), for assessment of the proprietary name, "*Pranactin-Citric*," regarding potential name confusion with other proprietary/generic drug names.

The sponsor currently markets a product with the proprietary name, *Pranactin*. Pranactin is a drug component of a currently marketed diagnostic kit, *Meretek UBT®*. The Meretek UBT is used in the noninvasive urea breath test for detection of *Helicobacter pylori*. The Meretek UBT® contains Pranactin, which contains **125 mg** of the diagnostic drug, ^{13}C-Urea. The Pranactin should be administered orally 30 minutes prior to the breath test. Pranactin must be reconstituted with 75 ml of sterile water. The urease produced by H. pylori decomposes ^{13}C-Urea to $^{13}CO_2$ and NH_4^+ in the highly acidic environment of the stomach. This $^{13}CO_2$ is absorbed into the blood and then exhaled in the breath. This results in an increase in the ratio of $^{13}CO_2$ to $^{12}CO_2$ in a test breath sample compared to a baseline sample taken before the Pranactin solution was consumed. An analysis of the breath samples is performed by Gas Isotope Ratio Mass spectrometry.

The sponsor, Meretek, applied for a supplement 004 to NDA 20-586 to "change the composition of the drug component, Pranactin." Furthermore, the sponsor requested to change the proprietary name from Pranactin to Pranactin-Citric. Initially, the sponsor requested to change the proprietary name of the device/drug combination product from Meretek UBT to Meretek [redacted] through CDRH. Then, the sponsor changed the name from "Meretek [redacted] to "BreathTek UBT." [redacted]

PRODUCT INFORMATION

Pranactin-Citric is the proposed proprietary name for ^{13}C-Urea and it is a drug component of *BreathTek UBT*. Pranactin-Citric is a new formulation of the currently marketed product, Pranactin. Pranactin-Citric contains the following ingredient:

75 mg of ^{13}C-Urea
— ng of citric acid
— g of aspartame
— g of mannitol.

BreathTek UBT Breath Test Collection Kit is intended for use in the qualitative detection of urease associated with *Helicobacter pylori* in the human stomach and as an aid in the initial diagnosis and post-treatment monitoring of *Helicobacter pylori* infection in adult patients. The test may be used for monitoring treatment if used at least four weeks following completion of H. Pylori therapy. Pranactin-Citric should be reconstituted with 120 mL of potable tap water. It needs to be administered 15 minutes prior to the breath sample. The urease produced by H. pylori decomposes ^{13}C-Urea to $^{13}CO_2$ and NH_4^+ in the highly acidic environment of the stomach. This $^{13}CO_2$ is absorbed into the blood and then exhaled in the breath. This results in an increase in the ratio of $^{13}CO_2$ to $^{12}CO_2$ in a test breath sample compared to a baseline sample taken before the Pranactin-Citric solution was consumed. An analysis of the breath samples is performed by Gas Isotope Ratio Mass spectrometry.

II. RISK ASSESSMENT

A. EXPERT PANEL DISCUSSION

Because Pranactin ® is a product name already in use in the U.S. marketplace, no prescription simulation studies were conducted.

The Expert Panel discussion was conducted by OPDRA to gather professional opinions on the safety of the proprietary name, *Prantin-Citric.* Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of OPDRA Medication Errors Prevention Staff and representation from the Division of Drug Marketing and Advertising Communications (DDMAC). The group relies on their clinical, regulatory, and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

A representative from DDMAC did not have any concerns about the name with regard to promotional claims.

B. SAFETY EVALUATOR RISK ASSESSMENT

In regard to the proposed name, *Pranactin-Citric*, we recognize that the modifier, "Citric", is used to distinguish the proposed product from the currently marketed product, *Pranactin.* This modifier, "Citric", is not appropriate for the following reasons:

The proposed product, *Pranactin-Citric*, contains the same active ingredient, ^{13}C-Urea, as the currently marketed product, *Pranactin.* However, *Pranactin-Citric* contains a different amount of ^{13}C-Urea than the currently marketed product, *Pranactin. Pranactin-Citric* contains 75 mg of ^{13}C-Urea instead of 125 mg contained in *Pranactin.* Moreover, *Pranactin-Citric* contains the inactive ingredients, — of citric acid, — of aspartame, and — of mannitol, not contained in the current product. The citric acid was added to Pranactin-Citric to "inhibit

gastric emptying." Consequently, the amount of ^{13}C-Urea has been decreased from 125 mg to 75 mg. Also, the citric acid "enhances the diagnostic signal." According to the chemist, Ravi Harapanhalli, "the citric acid is an inactive ingredient."

The modifier, "*Citric*", is used to place an emphasis on the citric acid, an inactive ingredient, contained in the proposed product. However, the proprietary name, Pranactin-Citric, places an emphasis on an inactive ingredient and this is in violation of 21 CFR 201.10 (c) (4):

> "The featuring in the labeling of inert or inactive ingredients in a manner that creates an impression of value greater than their true functional role in the formulation."

We acknowledge that the citric acid is the essential inactive ingredient that reduced the amount of ^{13}C-Urea from 125 mg to 75 mg, but the citric acid "inhibits gastric emptying." The active ingredient, ^{13}C-Urea, is the diagnostic drug and it decomposes to $^{13}CO_2$ and NH_4^+ in the highly acidic environment of the stomach. This $^{13}CO_2$ is absorbed into the blood and then exhaled in the breath, and the ratio of $^{13}CO_2$ to $^{12}CO_2$ is measured by the Gas Isotope Ratio Mass spectrometry.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In the review of the container label of Pranactin-Citric, OPDRA has attempted to focus on safety issues relating to possible medication errors. We have identified several areas of possible improvement, in the interest of minimizing potential user errors.

A. CONTAINER LABEL

1. Pranactin-Citric contains 75 mg of ^{13}C-Urea, which must be reconstituted with 120 mL of potable tap water. *We suggest that the established name of this product be revised* throughout the product labeling, based upon nomenclature practice in the USP/NF[i], to read '

2. Revise the usual dosage statement to read: "Usual Dosage: See Package Insert."

B. PACKAGE INSERT

No comments.

IV. RECOMMENDATIONS

1. OPDRA does not recommend the use of the proposed name, Pranactin-Citric.

2. OPDRA recommends implementation of the above labeling revisions to minimize potential errors with the use of this product.

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[i] USP 24/NF 19: U.S. Pharmacopeia and National Formulary, 1999, The United States Pharmacopeial Convention, Inc., Rockville, MD, p.2115, "Oral Solutions".

OPDRA would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Hye-Joo Kim, Pharm.D. at 301-827-0925.

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Office of Postmarketing Drug Risk Assessment (OPDRA)

Concur:

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APPEARS THIS WAY
ON ORIGINAL