CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-586/S-004

CHEMISTRY REVIEW(S)

SUPPLEMENTAL NDA CHEMIST'S REVIEW	1. ORGANIZATION: HFD-590	2. NDA NUMBER: 20-586

3. NAME AND ADDRESS OF APPLICANT: *(City and State)*
Meretek Diagnostics, Inc.
618 Grassmere Park Drive, Suite 20
Nashville, TN 37211

4. AF NUMBER:

5. SUPPLEMENT(S):

NUMBER(S):	DATE(S):
SE2-004	13-JUN-2000
SE2-004 NC	10-OCT-2000
SE2-004 BC	30-OCT-2000
SE2-004 BC	21-MAR-2001
SE2-004 BC	22-MAR-2001
SE2-004 BC	26-MAR-2001
SE2-004 BC	16-APR-2001
SE2-004 BL	19-APR-2001

6. NAME OF DRUG:
Pranactin-Citric™

7. NONPROPRIETARY NAME:
^{13}C-Urea

8. SUPPLEMENT PROVIDES FOR: A modified formulation of the diagnostic drug component of the device/drug diagnostic kit , the [redacted] Breath Test for H. pylori

9. AMENDMENTS/REPORTS:

10. PHARMACOLOGICAL CATEGORY:
Diagnostic

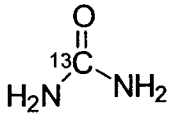
11. HOW DISPENSED:
[X] Rx [ ]OTC

12. RELATED IND/NDA/DMF(S):
510(k) #K000316

13. DOSAGE FORM(S):
Powder for solution (oral)

14. POTENCY(IES):
75 mg/unit

15. CHEMICAL NAME AND STRUCTURE: ^{13}C-urea



$^{13}CH_4N_2O$
Av. Mol. Wt.: 61.23

16. MEMORANDA:

OPDRA consult (labeling)

17. COMMENTS: See page 2.

18. CONCLUSIONS AND RECOMMENDATIONS: Meretek has submitted adequate information to assure the identity, strength, quality and purity of the product. APPROVAL of this supplement is recommended.

19. REVIEWER:	SIGNATURE:	DATE COMPLETED:
Gene W. Holbert, Ph.D.		
20. CONCURRENCE: Norman R. Schmuff, Ph.D.		

DISTRIBUTION:						
	X	Original NDA	X	HFD-590: NSchmuff	X	HFD-590: LChan
	X	Division File HFD-590	X	HFD-590: GHolbert	X	HFD-830: CChen

17. COMMENTS:

This supplement provides for a new diagnostic drug, Pranactin-Citric™, in support of the diagnostic kit, the ——— Breath Test for H. Pylori, which was approved in a Special 510(k) on February 24, 2000. Pranactin-Critic™ is a modified formulation of Pranactin®.

The original Pranactin® formulation consisted solely of ^{13}C-urea (125 mg), which was dissolved in water and administered following a commercially available pudding to inhibit gastric emptying. The new formulation, Pranactin-Citric™, consists of ^{13}C-urea (75 mg), citric acid, aspartame and mannitol as a dry powder for reconstitution with water. The current and proposed kits are compared in the following table.

Component	Meretek UBT®	Proposed Meretek UBT-Lite™
Drug Component	Pranactin® 125 mg ^{13}C-urea Vacuum dried powder	Pranactin-Citric™ 75 mg ^{13}C-urea Formulated dosage with citric acid, aspartame and mannitol
Container/Closure	Clear glass vial, lyophilization stopper and crimp overseal	Multi-layer, lined, foil laminate sealed in a continuous form-fill-seal operation to create a unit pouch.
Solvent for Reconstitution	75 mL sterile water added to drug component	120 mL potable tap water added to formulation in a dose cup
Pre-test Fast	4 hours	1.hour
Pretest Meal	Commercial pudding	No pretest meal. The citric acid serves to inhibit gastric emptying.
Specimen collection method	Plastic breath bag 4 evacuated test tubes (Baseline and post dose samples are collected in duplicate for back-up)	Straw 4 test tubes (The same tubes are used, but the stopper is removed, then replaced for the direct collection procedure.)
Specimen collection time (post-dose)	30 minutes	15 minutes

Each test kit contains a polymer lined foil pouch containing 3 g of Pranactin-Citric™ of the following composition:

Ingredient	Amount per Unit	Primary Function
^{13}C-urea	75 mg	Active drug
Aspartame	———	[ ]
Mannitol	———	
Citric acid, anhydrous	———	

The active ingredient is of the same quality and is obtained from the same manufacturers as that used in the current kit. All excipients are compendial.

[ ]

[redacted]

Batches Tested	Stability Testing Performed
[redacted]	

The data submitted to date do not support a [redacted] expiration date. The available data (15 months on one batch and 12 months on a second) would support at most an expiration date of [redacted] However, considering the known stability of urea ($t_{1/2}$ of 29 years at 25°C), the [redacted] month expiration date for the current product and NIST's recommended retest period of 5 years for samples stored at 25°C in a well-closed container, a [redacted] expiry period is appropriate.

Meretek claims a categorical exclusion from Environmental Assessment based on the estimation that any increase in use will not result in a concentration < 1 ppb at the point of entry into the aquatic environment. Approval of this supplement will likely result in decreased usage since the amount of active in the formulation is 40% lower.

The container label is the preprinted pouch and is generally acceptable. The package insert originally referred to mannitol as an inactive ingredient instead of by name. Ultimately, the firm was convinced to list mannitol by name.

The labeling was sent to OPDRA for consultation. OPDRA recommended against use of the proprietary name, Pranactin-Citric, because they felt that it was "the featuring in the labeling of inert or inactive ingredients [i.e., citric acid] in a manner that creates an impression of value greater than their true functional role in the formulation." (21 CFR 201.10(c)(4)) On the other hand, the Review Team felt that the name was acceptable because it was descriptive, did not create any impression of any added value and that citric acid was more than just an inactive ingredient *in this case.* The presence of citric acid delays the emptying of the stomach, allowing *H. pylori* urease to act on a greater portion of ^{13}C-Urea to give an "enhanced diagnostic signal" and permitting the decreased dosage.

Deficiencies noted during the review were communicated to the sponsor who has responded in an adequate fashion.

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