HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use IDKIT HP® ONE AND IDKIT HP® TWO safely and effectively. See full prescribing information for IDKIT HP® ONE AND IDKIT HP® TWO.

IDKIT HP® One (^{13}C-urea tablet for oral solution; Citrica (citric acid) for oral solution), co-packaged
IDKIT HP® Two (^{13}C-urea tablet for oral solution; Citrica (citric acid) for oral solution), co-packaged
Initial U.S. Approval: 2002

----------INDICATIONS AND USAGE----------

IDkit Hp One and IDkit Hp Two are indicated for use as a diagnostic aid in the initial diagnosis and post-treatment monitoring of *Helicobacter pylori* (*H. pylori)* infection in adults and pediatric patients 3 years of age and older. (1)
IDkit Hp One and IDkit Hp Two are to be administered only by trained personnel as ordered by a licensed healthcare practitioner using the BreathID® system device as identified in the BreathID® system device labeling. (1)

----------DOSAGE AND ADMINISTRATION----------

IDkit Hp One and IDkit Hp Two each contain a 75 mg ^{13}C-urea tablet for oral solution, and 4 g Citrica (citric acid) for oral solution along with other materials for use with the BreathID system device (2.1, 16)

- IDkit Hp One is co-packaged with a nasal canula to be used with the BreathID system device as identified in the BreathID system device labeling. (2.1)
- IDkit Hp Two is co-packaged with breath sample bags to be used with the BreathID system device as identified in the BreathID system device labeling. (2.1)

- To prepare the oral solution for either kit, dissolve the ^{13}C-urea tablet and the Citrica (citric acid) for oral solution in 150 to 200 mL of water to provide a clear, colorless solution for oral administration. The resulting solution is ingested by the patient. (2.3)
- See full prescribing information for detailed important instructions concerning preparation, administration, and disposal of IDkit Hp One and IDkit Hp Two. (2.3-2.6)
- See *BreathID® system device manua*l for additional details for use of IDkit Hp One and IDkit Hp Two with the BreathID system device, including troubleshooting device malfunction. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

75 mg ^{13}C-urea tablet for oral solution co-packaged with 4g Citrica (citric acid) for oral solution. (3)

----------CONTRAINDICATIONS----------

- Hypersensitivity to the ^{13}C-urea, Citrica (citric acid) or to any of the excipients in the drug. (4)

----------WARNINGS AND PRECAUTIONS----------

- Hypersensitivity Reactions: Hypersensitivity reactions, including anaphylaxis, have been reported in patients using IDkit Hp. Institute appropriate supportive measures if an allergic reaction occurs. (5.1)
- Phenylketonuria: Citrica (citric acid) for oral solution, a component in the IDkit Hp, contains phenylalanine which can be harmful to patients with phenylketonuria. (5.2)

.----------ADVERSE REACTIONS----------

- Adult Patients: The most common adverse reactions (incidence >0.3%) using the IDkit Hp included nausea, throat burning, and lightheadedness. (6.1)
- Pediatric Patients: The most common adverse reactions (incidence >1.5%) using the IDkit Hp included vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Meridian Bioscience Corporation at 1-800-543-1980 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

Antimicrobials, Bismuth-containing preparations: Avoid use within 2 weeks prior to testing. (7)
Proton pump inhibitors (PPIs): Avoid use within 2 weeks prior to testing. (7)

----------USE IN SPECIFIC POPULATIONS----------

Pediatric Use: The safety and effectiveness of IDkit Hp One and IDkit Hp Two has not been established in pediatric patients less than 3 years of age. (8.4)

See 17 for PATIENT COUNSELING INFORMATION

Revised 7/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

IDkit Hp® One and IDkit Hp® Two are indicated for use as a diagnostic aid in the initial diagnosis and post-treatment monitoring of *Helicobacter pylori* (*H. pylori)* infection in adults and pediatric patients 3 years of age and older.

IDkit Hp One and IDkit Hp Two are to be administered only by trained personnel as ordered by a licensed healthcare practitioner using the BreathID® system device as identified in the BreathID® system device labeling.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage and Administration Overview

- IDkit Hp One or IDkit Hp Two contain the same drug product, 75 mg ^{13}C-urea tablet and 4 g Citrica (citric acid) for oral solution and follow the same drug preparation and administration instructions.
- IDkit Hp One and IDkit Hp Two are to be administered only by trained personnel as ordered by a licensed healthcare practitioner, using the BreathID system device that as identified in the BreathID system device labeling, is intended for use with IDkit Hp One and IDkit Hp Two.
- For in vitro diagnostic use only.
- Inform the patient that each 4 g packet of Citrica (citric acid) for oral solution contains 84 mg of phenylalanine per dose. Phenylketonurics restrict dietary phenylalanine *[see Warnings and Precautions (5.2)]*.
- The patient should have fasted for at least one hour before administering the test drink.
- The patient should not have taken antimicrobials, proton pump inhibitors (PPI), or bismuth preparations within two weeks prior to administering the test. If PPIs are used within two weeks of breath testing, false negative test results may occur, and the test should be repeated two weeks after discontinuation of PPI treatment. A positive result for a patient on PPI could be considered as indicative of the presence of urease enzyme associated with *H. pylori*.
- Before opening the kit (IDkit Hp One or IDkit Hp Two), verify that the entire package is intact [*see How Supplied/Storage and Handling (16)*].

2.2 Recommended Dosage for Adults and Pediatric Patients 3 Years of Age and Older

IDkit Hp One Single-use Kit or IDkit Hp Two Single-use Kit

A 75 mg ^{13}C-urea tablet for oral solution and 4 g Citrica (citric acid) for oral solution are dissolved in 150 to 200 mL of water for oral consumption, and the resulting solution is ingested by the patient.

2.3 Preparation of IDkit Hp One Single-use kit or IDkit Hp Two Single-use Kit

Preparation Instructions with IDkit Hp One single-use kit or IDkit Hp Two single-use kit

1. Dissolve the ^{13}C-urea tablet and Citrica (citric acid) for oral solution in 150 mL to 200 mL of tap water in a single drinking cup of at least eight ounces (236 mL) in capacity.
    - In the IDkit Hp Two kit a drinking cup is provided.
2. Stir thoroughly with the provided straw until the ^{13}C-urea tablet and Citrica (citric acid) for oral solution are completely dissolved.

- Tiny particles may remain visible after thorough mixing. However, if more substantial particulate matter is still present after five minutes of stirring, discard the solution and repeat the procedure with a new kit.
- Use the test drink within two hours of preparation, as this is the maximal time for maintaining solution stability.

2.4 IDkit Hp One Single-use Kit: Instruction for Performing the BreathID *H. pylori* Test

Preparing the BreathID System Device

1. Refer to the BreathID system device labeling for additional details.
2. Ensure that the BreathID system device is activated, and the status is **Ready**. The status appears on the top right of the screen.
3. Follow the screen instructions
4. Connecting the IDcircuit®:
    a. Take the IDcircuit® out of its bag and slide the tubing sleeve down as far as it will go. Gently place the cannula tips into the patient's nostrils, and place the cannula tubing over the ears, as shown in Figure 1.

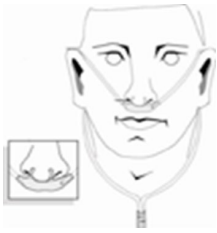


Figure 1

    b. Slide the tubing sleeve up towards the neck to fit comfortably under the chin.
    c. Connect the IDcircuit to the BreathID system device by twisting the orange connector at the free end of the cannula clockwise until it is secured into the dedicated socket of the BreathID system device.
    d. Verify that the IDcircuit is not twisted or kinked and that the cannula tips are in the nostrils. Ensure that the IDcircuit cannula tips moldings are positioned inwards.
    e. Press the START button on the touch screen to proceed. The baseline values will be measured by the BreathID system device, and the results will be shown on the screen.
5. Administering the Test Drink and Starting Measurement

    *Do **not** administer the test drink until prompted by the screen instructions on the device (this makes certain that the baseline sample has been collected properly).*
    a. Ensure that the patient drinks the solution through the straw.
    b. The patient, including pediatric patients 3 years of age and older, regardless of age and body weight, must drink the solution within two minutes and consume the entire amount.
    c. After the patient finishes drinking the solution, press the **Continue** button on the touch screen to proceed.
6. Measurement with the BreathID System Device
    a. The BreathID system device continually analyzes the trend of measured results. When the device determines that the final value will be positive or negative, i.e., greater or less than 5 Delta Over Baseline, it will automatically end the test and print out the results. The breath sample is analyzed in real-time by the BreathID system device; therefore, the stability of the final breath sample will not affect the outcome of the results.

7. Removing and Discarding the IDcircuit:
    a. When the measurement is complete, disconnect the IDcircuit from both the patient and the device. Dispose of the IDcircuit and all other used components of the kit according to standard operating procedures or local regulations for the disposal of used medical waste.
    If you do not disconnect the IDcircuit, instructions will appear on the device screen reminding you to do so. The device will not proceed to the next screen until the IDcircuit is disconnected.
8. Printing Results:
    a. After the measurement is complete, the device will automatically print the test results. The printout contains the graph as seen on the screen, including the Patient ID (if entered), date, time, test number, and Delta Over Baseline value of the last point measured.
    b. Tear off the printed results and fill in additional patient data as required.

2.5 IDkit Hp Two Single-use Kit: Instructions for Performing the BreathID *H. pylori* Test

1. Identify the two Breath Sample Bags (the blue BASELINE bag and the gray POST INGESTION bag).
2. Prior to sampling the patient's breath, label each bag with the supplied barcode labels or write the necessary identification information in the appropriate fields on each bag.
3. Collection of the BASELINE breath sample:
    a. Remove the cap from the mouthpiece of the blue BASELINE bag.
    b. Instruct the patient to take a deep breath, hold their breath for 4 to 5 seconds and then exhale directly into the mouthpiece of the blue BASELINE breath bag until completely full.
    c. If the bag is not full, repeat step b.
    If the patient has not held their breath for 4-5 seconds or does not fill the bag completely, there is a possibility that a test result will not be obtainable.
    d. Replace the cap on the bag mouthpiece and firmly press until it clicks and is securely locked into place.
    The bag is not fully closed if the cap does not click into place. Not fully closing the bag may cause the breath sample to slowly leak out.
4. Administering the test drink:
    a. Give the prepared test drink to the patient.
    b. Ensure that the patient drinks the solution through the provided straw.
    c. The patient, including pediatric patients 3 years of age and older, regardless of age and body weight, must drink the solution within two minutes and consume the entire amount.
    d. Start the timer for 15 minutes.
    e. After the patient finishes drinking the solution, record the present time plus (+) another 15 minutes in the Time to Fill field on the gray POST INGESTION bag.
5. Collection of the POST INGESTION breath sample:
    a. Fifteen minutes after the administration of the test drink (but not later than 20 minutes after administration) remove the cap from the mouthpiece of the gray POST INGESTION bag.
    b. Instruct the patient to take a deep breath, hold their breath for 4 to 5 seconds, and then exhale directly into the mouthpiece of the gray POST INGESTION bag until it is full.
    c. If the bag is not full, repeat step b.

Note: *If the patient has not held their breath for 4-5 seconds or does not fill the bag completely, there is a possibility that a test result will not be obtainable*

d. Replace the cap on the bag mouthpiece and firmly press until it clicks and is securely locked into place.

Note: *The bag is not fully closed if the cap does not click into place. Not fully closing the bag may cause the breath sample to slowly leak out.*

6. Storage of Breath Sample Bags for future measurement:
    a. Assure both filled Breath Sample Bags are correctly labeled, and all fields are complete for future identification.
    b. Place both filled Breath Sample Bags (the blue BASELINE bag and the gray POST INGESTION bag) into the provided sample transport bag.
    c. Until analyzed, Breath Sample Bags should be stored at room temperature (15°C to 30°C, 59°F to 86°F), protected from direct sunlight and sharp objects. Refrain from applying any external pressure on the Breath Sample Bags.

2.6 Interpretation of Results and Retesting

- Refer to the BreathID system device labeling for additional details.
- A negative result does not rule out the possibility of *H. pylori* infection. False negative results can occur with this procedure. If clinical signs suggest *H. pylori* infection, retest with a new sample or an alternate method.
- A false positive test may occur due to urease associated with other gastric spiral organisms observed in humans, such as *Helicobacter heilmanni*.
- A false positive test could occur in patients who have achlorhydria.
- False negative test results may be caused by:
    - Ingestion of antimicrobials or bismuth preparations within two weeks prior to performing the breath test.
    - Ingestion of proton pump inhibitors (PPIs) within two weeks prior to performing the breath test.
    - *If a negative result is obtained from a patient ingesting a PPI within two weeks prior to the breath test, the results cannot be considered indicative of the absence of urease associated with H. pylori, and the test should be repeated two weeks after discontinuing the PPI treatment. A positive result for a patient on a PPI could be considered as indicative of the presence of urease associated with H. pylori.*
- Post-treatment monitoring of *H. pylori* should be performed after at least six weeks of treatment for *H. pylori* infection. An earlier assessment may give false results.

3 DOSAGE FORMS AND STRENGTHS

IDkit Hp One and IDkit Hp Two consists of a ^{13}C-urea tablet for oral solution co-packaged with Citrica (citric acid) for oral solution along with other materials for use with the BreathID system device *[see How Supplied/Storage and Handling (16)]*.

^{13}C-urea tablet for oral solution is supplied as a white, biconvex round tablet with "U" debossed on one side. Each tablet contains 75 mg ^{13}C-urea.

Citrica (citric acid) for oral solution is supplied as a white to off-white powder. Each pouch contains 4 grams of citric acid.

4 CONTRAINDICATIONS

IDkit Hp One and IDkit Hp Two are contraindicated in patients with a known hypersensitivity to the ^{13}C-urea, Citrica (citric acid) or to any of the excipients *[see Warnings and Precautions (5.1) and Adverse Reactions (6.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis, have been reported in patients who have used the IDkit Hp One and IDkit Hp Two for *H. pylori* diagnostic testing *[see Adverse Reactions (6.2)]*. The IDkit Hp One and IDkit Hp Two are contraindicated in patients with known history of hypersensitivity to ^{13}C-urea, Citrica (citric acid) or the excipients *[see Contraindications (4)]*. Before administering the IDkit Hp One or IDkit Hp Two, carefully inquire about previous hypersensitivity reactions.

5.2 Risks in Patients with Phenylketonuria

Phenylalanine can be harmful to patients with phenylketonuria (PKU). In IDkit Hp One and IDkit Hp Two, the Citrica (citric acid) for oral solution contains phenylalanine, a component of aspartame. Each 4 g packet of Citrica (citric acid) for oral solution contains 84 mg of phenylalanine. Before prescribing IDkit Hp One or IDkit Hp Two to a patient with PKU, consider the combined daily amount of phenylalanine from all sources, including IDkit Hp One or IDkit Hp Two.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in the Warning and Precautions section of the labeling:

- Hypersensitivity Reactions *[see Warning and Precautions (5.1)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials Experience and Adverse Reactions in Adult Patients

The safety of the IDkit Hp was evaluated in 465 adult patients who participated in two clinical trials (Trial 1 and Trial 2). All patients used the IDkit Hp Two kit for initial diagnosis and post-treatment monitoring of *H. pylori* infection. The most commonly observed adverse reactions associated with the use of the IDkit Hp were nausea (0.6%), throat burning (0.4%), and lightheadedness (0.4%).

Clinical Trials Experience and Adverse Reactions in Pediatric Patients

The safety of the IDkit Hp was evaluated in one multi-center, non-randomized, open-label study (Trial 3). A total of 53 pediatric patients, 3 to less than 18 years of age, were enrolled in the study and used the IDkit Hp Two. The only adverse reaction reported was vomiting (2%).

6.2 Post-marketing Experience

In addition to adverse reactions reported from clinical trials, the following adverse reactions have been identified during post-marketing use of the IDkit Hp One and IDkit Hp Two based on patient and test administrator reports. Because these reactions are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal: Nausea, vomiting, abdominal pain, diarrhea

General: Sweating, throat pain, malaise

Immune: Anaphylactic reaction

Neurologic: Dizziness, headache

7 DRUG INTERACTIONS

No formal drug interaction studies were conducted. Information on drugs that may interfere with test results are listed in the Table 1.

Table 1: Drugs That Interfere with Test Results

Interfering Drug	Clinical Effect	Prevention or Management
Antimicrobials, bismuth-containing preparations	May suppress *H. pylori* or urease activity, leading to false negative results	Avoid use within 2 weeks prior to testing. If used within 2 weeks, postpone testing until at least 2 weeks after discontinuation.
Proton pump inhibitors (PPIs)	May reduce urease activity or alter gastric conditions, potentially causing false negative results. A positive result during PPI use may still indicate *H. pylori* presence.	Avoid use within 2 weeks prior to testing. If a negative result is obtained during PPI use, repeat the test 2 weeks after PPI discontinuation.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Published data from other single oral dose ^{13}C-urea breath test kits containing urea and citric acid have not demonstrated a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. There are no available data on the use of IDkit Hp One or IDkit Hp Two use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. There are no animal data that meet current standards for nonclinical developmental toxicity studies. Based on available literature, no significant developmental or reproductive toxicities were observed in nonclinical studies with urea or citric acid. A single oral dose of ^{13}C-urea and citric acid at the maximum recommended human dose (MRHD) are unlikely to pose a significant developmental or reproductive risk, since humans typically have higher circulating levels of urea, and citric acid exposure from the test is within the range of normal dietary intake.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the U.S. general population, the background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

8.2 Lactation

Risk Summary

There are no data on the presence of the components of IDkit Hp One or IDkit Hp Two in either human or animal milk, the effects on the breastfed infant, or the effects on milk production. A single oral dose of ^{13}C-urea and citric acid at the MRHD is unlikely to pose a risk in breastfed infants since humans typically have higher circulating levels of urea, and citric acid exposure from the test is within the range of normal dietary intake.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IDkit Hp One or IDkit Hp Two and any potential adverse effects on the breastfed infant from IDkit Hp One or IDkit Hp Two or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of IDkit Hp One and IDkit Hp Two have been established in pediatric patients 3 years of age and older. Use of IDkit Hp One and IDkit Hp Two in pediatric patients is supported by two trials demonstrating clinical performance in adults along with a multi-center, non-randomized, open label study confirming the safety of the ^{13}C-urea substrate and the performance of the BreathID system device in pediatric patients *[see Adverse Reaction (6.1) and Clinical Studies (14.1)].*

The safety and effectiveness of IDkit Hp One and IDkit Hp Two have not been established in pediatric patients less than 3 years of age.

8.5 Geriatric Use

Of the total number of IDkit Hp One and IDkit Hp Two patients in clinical studies for detection of *H. pylori*, 74 (12%) were 65 to 74 years of age, and 38 (6%) were 75 years of age and older *[see Clinical Studies (14)]*.No overall differences in safety or effectiveness were observed between patients 65 years of age and older and younger adult patients, and other reported clinical experience has not identified differences in responses between the elderly and younger adult patients.

8.6 Gastrectomy

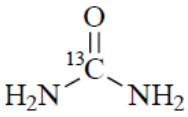
Data is insufficient for recommending the use of IDkit Hp One and IDkit Hp Two on patients with total or partial gastrectomy *[see Clinical Pharmacology (12.3)].*

11 DESCRIPTION

IDkit Hp One and IDkit Hp Two are a diagnostic aid that analyzes a breath sample before and after ingestion of ^{13}C-urea and citric acid; it is used to identify those patients with a *H. pylori* infection. The kit consists of a ^{13}C-urea tablet for oral solution and Citrica (citric acid) for oral solution along with other materials for use with the BreathID system device *[see How Supplied/Storage and Handling (16)].*

^{13}C-Urea Tablet for Oral Solution

^{13}C-urea has a molecular weight of 61.06 g/mol and the molecular formula $^{13}CH_4N_2O$ and the following structure:



^{13}C-urea tablet for oral solution contains 75 mg ^{13}C-urea and the following inactive ingredients: colloidal silicon dioxide, microcrystalline cellulose, povidone, and sodium benzoate.

Citrica (citric acid) for Oral Solution

Citric acid has a molecular weight of 210.14 g/mol and the molecular formula $C_6H_8O_7$. Each pouch contains 4 g of citric acid and the following inactive ingredients: aspartame and tutti frutti flavoring.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

IDkit Hp One and IDkit Hp Two are administered using the BreathID system device, a non-invasive breath test that analyzes a breath sample before and after ingestion of ^{13}C- urea and citric acid. 75 mg ^{13}C-urea and 4. g citric acid is dissolved in water and administered orally to the patient. The presence of citric acid creates an acidic environment in the stomach and delays the gastric emptying of the ingested solution to the duodenum. These two characteristics facilitate the decomposition of the urea by *H. pylori*, if present. Thus, in the presence of urease produced by gastric *H. pylori*, ^{13}C-urea is decomposed to $^{13}CO_2$ and NH_3 according to the following equation:

$$^{13}\text{C Urea} + H_2O \xrightarrow{\text{urease}} {}^{13}CO_2 + 2\ NH_3$$

The $^{13}CO_2$ formed is absorbed into the blood and then exhaled in breath, enabling detection of elevated $^{13}CO_2$ in *H. pylori-positive* patients.

In *H. pylori*-negative patients, no significant production of $^{13}CO_2$ occurs in the stomach, as there are no human enzymes capable of hydrolyzing urea under gastric conditions.

12.2 Pharmacodynamics

IDkit Hp One and IDkit Hp Two (^{13}C-urea and citric acid) have no therapeutic pharmacodynamic effects. It contains diagnostic agents ^{13}C-urea and citric acid that detects the presence of *H. pylori* based on bacterial urease activity in the gastric mucosa.

12.3 Pharmacokinetics

Absorption

Following oral administration of ^{13}C-urea 100 mg to 400 mg (1.33 to 4 times the highest approved recommended dosage) in 3 healthy subjects, the Tmax of ^{13}C-urea was around 30 minutes *[see Dosage and Administration (2.1)]*.

Elimination

Metabolism

In *H. pylori*-positive subjects, ^{13}C-urea is hydrolysed in the stomach by bacterial urease to $^{13}CO_2$ and ammonia.

Excretion

Urea is eliminated predominantly by renal excretion.

Specific Populations

The pharmacokinetics of ^{13}C-urea are not expected to have clinically meaningful differences based on age (including geriatric and pediatric patients), sex, race, or ethnicity with respect to its activity as diagnostic agent.

Gastrectomy Patients

The performance and reliability of the test in gastrectomy patients have not been established.

Drug Interaction Studies

No formal drug interaction studies have been conducted. Antimicrobials, proton pump inhibitors, and bismuth preparations may affect *H. pylori* status or urease activity and interfere with test results *[see Drug Interactions (7)]*.

In vitro studies demonstrated that mouthwash, chewing gum, carbonated beverages, cigarette smoke, acetone, and alcohol had no clinically relevant effect on test results.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Carcinogenicity studies have not been conducted with ^{13}C-urea. No evidence of carcinogenicity of citric acid was observed in a 2-year study in male rats receiving doses up to 2,000 mg/kg/day. Single oral doses of urea and citric acid are not expected to be carcinogenic in humans.

Mutagenesis

Based on available literature, urea was negative in the Ames test and in vitro micronucleus assay in mouse lymphoma cells. In vitro and in vivo chromosomal aberration studies have demonstrated inconsistent results with urea, with limited study details available for comprehensive evaluation. Citric acid was also negative in the Ames test and in vitro chromosomal aberration assays.

Impairment of Fertility

The available nonclinical data are insufficient to determine whether ^{13}C-urea may have effects on fertility. Based on available literature, no significant effects on fertility were observed in nonclinical studies with citric acid. Single oral doses of urea and citric acid are not expected to impair fertility in humans.

14 CLINICAL STUDIES

14.1 IDkit Hp One

Adult Patients

Trial 1 was a prospective, open-label clinical trial conducted at two U.S. hospitals to assess the performance of the original BreathID test with the IDkit Hp One. The study was designed to assess the sensitivity and specificity of the test for determining the status of gastrointestinal infections with *H. pylori* compared to other methods (pre-therapy phase) and evaluate the ability of the system to monitor the efficacy of therapy for *H. pylori* (post-therapy phase).

The study enrolled 315 adult patients in the pre-therapy phase. The post-therapy phase included 77 patients who had been positive for infection and had undergone eradication therapy at least four weeks prior. Patients

were evaluated by at least two of the following diagnostic methods: histology, rapid urease test (RUT), and for post-therapy patients, an FDA-cleared urea breath test (UBT).

For the pre-therapy phase, the performance of the BreathID test with the IDkit Hp One was compared to congruent results from two endoscopy biopsy-based methods (RUT and histology). Performance was also compared to each method individually. Table 2 shows the congruent results from the two endoscopy biopsy-based methods (RUT and histology) compared to the original BreathID results. Overall, the observed sensitivity of the original BreathID test with the IDkit Hp One was 100% (95% CI: 92.5; 100.0). Table 3 shows the comparison between the rapid urease test results and the BreathID results. Table 4 shows the comparison between the histology results and the BreathID results.

Table 2: Comparison of the Original BreathID Test to Congruent Endoscopic Tests (RUT and histological exam) Pre-Therapy

	Original BreathID Test		
Congruent Endoscopic Tests*	Positive	Negative	Total
Positive	47	0	47
Negative	2	251	253
Total	49	251	300

**H. pylori positive is defined as positive rapid urea test and positive histology.*

**H. pylori negative is defined as negative rapid urea test and negative histology.*

Sensitivity: 100% [95% CI (92.5, 100)]

Specificity: 99.2% [95% CI (97.2, 99.9)]

Table 3: Comparison of the Original BreathID Test to Rapid Urease Test (RUT) Pre-Therapy

	Original BreathID Test		
RUT	Positive	Negative	Total
Positive	50	0	50
Negative	2	259	261
Total	52	259	311

% positive agreement: 100% [95% CI (94.2, 100)]

% negative agreement: 99.2% [95% CI (97.3, 99.9)]

Table 4: Comparison of the Original BreathID Test to Histology Pre-Therapy

	Original BreathID Test		
Histology	Positive	Negative	Total
Positive	47	2	49
Negative	6	251	257
Total	53	253	306

% positive agreement: 95.9% [95% CI (86.0, 99.5)]

% negative agreement: 97.7% [95% CI (95.0, 99.1)]

For the post-therapy phase, the performance of the original BreathID test with the IDkit Hp One was compared to results from two endoscopy biopsy-based methods (RUT and histology). The BreathID test

results were also compared to each method individually. Table 5 shows the results from the two endoscopy biopsy-based methods (RUT and histology) compared to the original BreathID results.

Table 6 shows the comparison between the rapid urease test results and the BreathID results. Table 7 shows the comparison between the histology results and the BreathID results. Table 8 shows the comparison between the UBT post-therapy results and the BreathID results.

Table 5: Comparison of Original BreathID Test to Endoscopic Tests (RUT and Histology) Post-Therapy

	Original BreathID Test		
Endoscopic Tests*	Positive	Negative	Total
Positive	6	0	6
Negative	0	20	20
Total	6	20	26

** H. pylori positive is defined as positive RUT and positive Histology*

**H. pylori negative is defined as negative RUT and negative Histology*

% positive agreement: 100% [95% CI (60.7, 100)]

% negative agreement: 100% [95% CI (86.1, 100)]

Table 6: Comparison of the Original BreathID Test to RUT Post-Therapy

	Original BreathID Test		
RUT	Positive	Negative	Total
Positive	7	0	7
Negative	0	21	21
Total	7	21	28

% positive agreement: 100% [95% CI (65.2, 100)]

% negative agreement: 100% [95% CI (86.7, 100)]

Table 7: Comparison of the Original BreathID Test to Histology Post-Therapy

	Original BreathID Test		
Histology	Positive	Negative	Total
Positive	6	0	6
Negative	1	20	21
Total	7	20	27

% positive agreement: 100% [95% CI (60.7, 100)]

% negative agreement: 95.2% [95% CI (76.2, 99.9)]

Table 8: Comparison of the Original BreathID Test to UBT Post-Therapy

	Original BreathID Test		
UBT	Positive	Negative	Total
Positive	14	1	15
Negative	0	31	31

Total	14	32	46

% positive agreement: 93.3% [95% CI (68.1, 99.8)]
% negative agreement: 100% [95% CI (90.8, 100)]

Table 9 compares the original BreathID to congruent results from the two biopsy-based methods (rapid urease test and histological exam) or the urea breath test.

Table 9: Comparison of the Original BreathID Test to Endoscopic Tests and/ or UBT Post-Therapy

	Original BreathID Test		
Endoscopic Tests and UBT*	Positive	Negative	Total
Positive	20	1	21
Negative	0	50	50
Total	20	51	71

**H. pylori positive is defined as either positive RUT and positive Histology, or positive UBT.*
**H. pylori negative is defined as either negative RUT and negative Histology, or negative UBT.*
% positive agreement: 95.2% [95% CI (76.2, 99.9)]
% negative agreement: 100% [95% CI (94.2, 100)]

Trial 2 was a single-center, one-arm, blinded, comparative study conducted to demonstrate the clinical equivalence of the modified BreathID test with the IDkit Hp One compared to the original BreathID test with the IDkit Hp One. The study included a total of 79 adult patients who were connected simultaneously to both devices. The outcome measures of both devices were used for the comparison. Overall, the observed positive agreement of the BreathID test with the IDkit Hp One compared to the original BreathID test was 100% (95% CI: 81.6; 100.0). Table 10 details the comparison between both systems.

Table 10: Comparison of the Modified BreathID Test to the Original BreathID Test

	Original BreathID Test		
Modified BreathID Test	Positive	Negative	Total
Positive	17	2	19
Negative	0	60	60
Total	17	62	79

**H. pylori positive is defined as positive on the original BreathID test.*
% positive agreement: 100% [95% CI (81.6, 100)]
% negative agreement: 96.8% [95% CI (89.0, 99.1)]

Pediatric Patients

Trial 3 was a multi-center, non-randomized, open-label study conducted to confirm the safety of the ^{13}C-urea substrate in IDkit Hp One and evaluate the performance of the BreathID system device in pediatric patients from 3 years to less than 18 years old (NCT02528721). The study was designed to assess the performance of the BreathID system and IDkit Hp One with nasal cannula to detect *H. pylori* utilizing a 5 delta over baseline (DOB) diagnostic cut-off compared to an FDA-cleared *H. pylori* stool antigen test.

A total of 41 pediatric patients were enrolled in the study across 6 clinical sites. Table 11 presents the diagnosis as assessed by the BreathID system using IDkit Hp One compared to the assessment by an FDA cleared *H. pylori* stool antigen test.

Table 11: Comparison of the BreathID Test using IDkit Hp One to an FDA-cleared *H. pylori* stool antigen test

	BreathID Test Using IDkit Hp One		
Stool Antigen	Positive	Negative	Total
Positive	14	1	15
Negative	0	26	26
Total	14	27	41

% positive agreement: 93.3% [95% CI (68.05, 99.83)]
% negative agreement: 100% [95% CI (86.77, 100)]

14.2 IDkit Hp Two

Adult Patients

Trial 4 was a multi-center, non-randomized, open-label validation study to confirm the efficacy of the IDkit Hp Two as part of the BreathID system for initial diagnosis and post-eradication testing (NCT02528721). The study was designed to assess the sensitivity and specificity of the test for determining the status of gastrointestinal infections with *H. pylori* compared to other methods (pre-therapy phase) and evaluate the ability of the system to monitor the efficacy of therapy for *H. pylori* (post-therapy phase). Efficacy was measured based on the results of the BreathID system with a 5 DOB diagnostic cut-off compared against a composite reference method of two endoscopy biopsy-based methods (RUT and histology). The stability of breath samples in the collection bags was also assessed by analyzing samples up to 14 days apart.

The study enrolled 196 adult patients for initial diagnosis and 76 post-therapy patients who were positive for infection and had completed eradication therapy at least six weeks prior to study recruitment. The study was conducted across 11 clinical sites in the United States and 2 clinical sites in Israel.

For the pre-therapy phase, the performance of the BreathID system using IDkit Hp Two was compared to composite results from two endoscopy biopsy-based methods (RUT and histology). Performance was also compared to each method individually. Table 12 shows the composite result from RUT and histology compared to the BreathID system using IDkit Hp Two. Overall, the observed sensitivity of the BreathID system using IDkit Hp Two was 100% (95% CI: 90.6; 100.0).

Table 13 and Table 14 compare the BreathID test using IDkit Hp Two to rapid urease tests (RUT) and histological exams, respectively.

Table 12: Comparison of the BreathID Test using IDkit Hp Two to Composite Reference Method (RUT and histological exam) Pre-Therapy

	BreathID Test Using IDkit Hp Two		
Composite Reference Method*	Positive	Negative	Total
Positive	37	0	37
Negative	3	139	142
Total	40	139	179

**H. pylori positive is defined as positive rapid urea test and positive histology.*
**H. pylori negative is defined as negative rapid urea test and negative histology.*
Sensitivity: 100% [95% CI (90.60; 100.00)]
Specificity: 97.9% [95% CI (93.97; 99.28)]

Table 13: Comparison of the BreathID Test using IDkit Hp Two to Rapid Urease Test (RUT) Pre-Therapy

	BreathID Test Using IDkit Hp Two		
RUT	Positive	Negative	Total
Positive	37	5	42
Negative	7	140	147
Total	44	145	189

Percent Positive Agreement: 88.1% [95% CI (75.00; 94.81)]
Percent Negative Agreement: 95.2% [95% CI (90.50; 97.67)]

Table 14: Comparison of the BreathID Test using IDkit Hp Two to Histology Pre-Therapy

	BreathID Test Using IDkit Hp Two		
Histology	Positive	Negative	Total
Positive	41	1	42
Negative	3	144	147
Total	44	145	189

Percent Positive Agreement: 97.6% [95% CI (87.68; 99.58)]
Percent Negative Agreement: 98.0% [95% CI (94.17; 99.30)]

For the post-therapy phase, the results of the BreathID test with the IDkit Hp Two were compared to a composite result from two endoscopy biopsy-based methods (RUT and histology) after patients completed eradication therapy. Table 15 compares the BreathID test to the composite reference method (rapid urease test and histological exam). The sensitivity of the BreathID test using IDkit Hp Two was 92.3% (95% CI: 66.9; 98.6) compared to the composite result. Table 16 and Table 17 compare the BreathID test using IDkit Hp Two to rapid urease tests (RUT) and histological exams, respectively.

Table 15: Comparison of the BreathID Test using IDkit Hp Two to Composite Reference Method Post-Therapy

	BreathID Test Using IDkit Hp Two		
Composite Reference Method*	Positive	Negative	Total
Positive	12	1	13
Negative	0	55	55
Total	12	56	68

**H. pylori positive is defined as positive RUT or positive Histology*
**H. pylori negative is defined as negative RUT and negative Histology*
Sensitivity: 92.3% [95% CI (66.69; 98.63)]
Specificity: 100% [95% CI (93.47; 100.00)]

Table 16: Comparison of the BreathID Test using IDkit Hp Two to RUT Post-Therapy

	BreathID Test Using IDkit Hp Two		
RUT	Positive	Negative	Total
Positive	11	0	11
Negative	1	56	57
Total	12	56	68

Percent Positive Agreement: 100% [95% CI (74.12; 100)]
Percent Negative Agreement: 98.25% [95% CI 90.71; 99.69)]

Table 17: Comparison of the BreathID Test using IDkit Hp Two to Histology Post-Therapy

	BreathID test using IDkit Hp Two		
Histology	Positive	Negative	Total
Positive	12	1	13
Negative	0	55	55
Total	12	56	68

Percent Positive Agreement: 92.3% [95% CI (66.69; 98.63)]
Percent Negative Agreement: 100% [95% CI (93.47; 100)]

Pediatric Patients

Trial 5 was a multi-center, non-randomized, open-label study conducted to confirm the safety of the ^{13}C-urea substrate in IDkit Hp Two and evaluate the performance of the BreathID system with IDkit Hp Two breath bags in pediatric patients from 3 years to less than 18 years old (NCT02528721). The study was designed to assess the performance of the BreathID system and IDkit Hp Two with breath sample bags, to detect *H. pylori* utilizing a 5 delta over baseline (DOB) diagnostic cut-off to an FDA-cleared *H. pylori* stool antigen test.

A total of 42 pediatric patients were enrolled in the study across 6 clinical sites. Table 18 presents the diagnosis as assessed by the BreathID system using IDkit Hp Two compared to the assessment by an FDA cleared *H. pylori* stool antigen test.

Table 18: Comparison of the BreathID Test using IDkit Hp Two to an FDA-cleared *H. pylori* stool antigen test

	BreathID Test using IDkit Hp Two		
Stool Antigen	Positive	Negative	Total
Positive	14	1	15
Negative	0	27	27
Total	14	28	42

Percent Positive Agreement: 93.3% [95% CI (68.05; 99.83)]
Percent Negative Agreement: 100% [95% CI (87.23; 100)]

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

IDkit Hp One and IDkit Hp Two each contain a 75 mg ^{13}C-urea tablet for oral solution and 4 g Citrica (citric acid) for oral solution along with other materials for use with the BreathID system device.

IDkit Hp® One NDC 50402-100-13

A single IDkit Hp One is provided to perform the Breath Test. Each IDkit Hp One contains:

- One ^{13}C-urea tablet for oral solution
- One packet of Citrica (citric acid) for oral solution
- One IDcircuit® nasal cannula
- One straw for stirring and drinking

Materials Needed but Not Provided:

- A drinking cup with a capacity of eight ounces (236 mL) or greater.
- Tap water

IDkit Hp® Two NDC 50402-100-14

A single IDkit Hp Two is provided to perform the Breath Test. Each IDkit Hp Two contains:

-
- One ^{13}C-urea tablet for oral solution
- One packet of Citrica (citric acid) for oral solution
- One straw for drinking
- One drinking cup
- One blue BASELINE Breath Sample Bag for BASELINE breath collection prior to ingestion of the test substrate
- One gray POST INGESTION Breath Sample Bag for 15 minutes POST INGESTION breath collection
- One large sample transport bag provided to store/ship both Breath Sample Bags
- Four barcode labels (one for each Breath Sample Bag and two for the requisition form)
- One Quick User Guide showing the basic steps of administering the test (printed on the inside of the box)

Materials Needed but Not Provided:

- Tap water
- Timer

16.2 Storage and Handling

Store at 20°C to 25°C (68°F-77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. The following components of the test kit have expiration dates: the ^{13}C-urea tablet and the Citrica Powder. Do not use either of these components beyond the expiration date stated on the respective labels. The earlier of the two expiry dates appears on the IDkit Hp box.

17 PATIENT COUNSELING INFORMATION

Important Administration Instructions

Advise patients, their families, or caregivers that the patient should stop taking antimicrobials, proton pump inhibitors (PPI), or bismuth preparations at least two weeks prior to administering the test *[see Dosage and Administration (2.1)]*.

Hypersensitivity Reactions

Advise patients, their families, or caregivers that serious hypersensitivity reactions, including anaphylaxis, could occur with use of ^{13}C-urea, Citrica (citric acid) or the excipients that require immediate treatment. Ask patients about any previous hypersensitivity reaction to ^{13}C-urea, Citrica (citric acid) or the excipients *[see Warnings and Precautions (5.1)]*.

Phenylketonuria

Advise patients with phenylketonuria that each 4 g packet of Citrica (citric acid) for oral solution contains 84 mg of phenylalanine. Phenylalanine can be harmful to patients with phenylketonuria. Contact your physician or pharmacist when prescribed the IDkit Hp One or the IDkit Hp Two *[see Warnings and Precautions (5.2)]*.

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For the most recent prescribing information about IDkit Hp® One and IDkit Hp® Two test kit, go to https://www.meridianbioscience.com/BreathID