H. pylori BreathTek® UBT

CLINICAL BACKGROUND

H. pylori is one of the most common bacterial infections in humans; 30%-40% of the US population is infected. Infection is thought to be acquired in childhood and may persist indefinitely without symptoms. Infection can also be acquired from infected persons living in close proximity. H. pylori causes 75%-80% of the Peptic Ulcer Disease (PUD) cases. In the U.S. there are more than 6 million cases annually resulting in an annual cost of $6 billion.1,2 Patients infected with H. pylori have a higher risk of developing gastric cancer. **May 2012 Lancet article states "H. pylori is one of six common infections that lead to cancer—it is preventable with early detection".

Per guidance, symptomatic patients who have infection should be treated with antibiotics and retested after antibiotic therapy to determine eradication of the organism.

CLINICAL APPLICATION

Patient conditions which warrant testing:

- Uninvestigated dyspepsia
- Duodenal or gastric ulcer (past or current)
- Atrophic gastritis
- Gastric malignancy
- Determine eradication success (test of cure)

Testing strongly recommended in these circumstances:

- Chronic use of NSAID, aspirin, or anti-secretory drug therapy
- Relatives of patients with H. pylori infection or peptic ulcer
- Non-ulcer dyspepsia with no alarm symptoms

Testing for H. pylori was previously done by serology, but this is no longer recommended because of its low sensitivity and inability to confirm eradication after therapy.2 Post therapy confirmatory testing is critical because 30% of patients fail to clear the organism after initial triple therapy.3 These patients require further evaluation and treatment.

The American College of Gastroenterology (ACG) and American Gastroenterological Associations (AGA) recommend, "test, treat, and retest to confirm eradication in patients with non-ulcer dyspepsia who are younger than age 55 and have no alarm symptoms."1,2 To avoid false negative results, post treatment testing should be delayed until 4 weeks after completion of the drug regimen.

BreathTek® UBT is simple to perform and uses a balloon collection device. The patient first provides a baseline sample, and then drinks a citrus flavored, non-radioactive 13C-Urea solution. 15 minutes later, a second breath sample is collected.

Conforms to the AGA, and the ACG guidelines for diagnosis and treatment.

- Both AGA and ACG recommend test and treat strategy for patients ≤55 who do not have alarm features.
- FDA cleared to test for cure.
- BreathTEK® tests for ACTIVE DISEASE – serology does not.
- 95% sensitivity.
- Non-invasive.
- Non-radioactive, stable isotope.
- May continue H2 antagonists through testing.
- FDA approved for adults and for pediatric patients age 3 to 17.
- H. pylori is estimated to be the cause of >90% of duodenal ulcers and up to 80% of gastric ulcers.

SELECTED REFERENCES

1. American College Gastroenterology Guidelines for Management of Dyspepsia, AJG,2005

www.paml.com
### TECHNICAL INFORMATION

- Patients should discontinue PPIs (includes Prilosec, Prevacid, Aciphex, Nexium), antibiotics and preparations containing bismuth (Pepto-Bismol), 2 weeks before diagnostic testing and 4 weeks before post treatment testing. The test is approved for initial testing on patients who may have taken PPIs within 2 weeks prior to a test. A positive result can be considered positive and acted upon. If negative, it is recommended to stop PPIs for 2 weeks and repeat test.
- H2 antagonists may be substituted for PPIs. These medications do not affect test results and include Zantac, Tagamet, Pepcid and Aixd.
- Patients should be NPO for one hour before the test is done (no food, liquids, or smoking). The test may not be suitable for patients with Phenylketonuria whose dietary phenylalanine should be restricted.
- Age, gender, height and weight information required for patients age 3 to 17.

### TEST INFORMATION

<table>
<thead>
<tr>
<th>DESCRIPTION</th>
<th>Helicobacter pylori Breath Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>METHOD</td>
<td>Infrared spectrophotometry</td>
</tr>
<tr>
<td>ORDER CODES</td>
<td>HPBRT (Peds) HPBTAD (Adults)</td>
</tr>
<tr>
<td>CPT CODES</td>
<td>83013, 83014 (sample collection)</td>
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</tbody>
</table>

**Patient Prep:** Patient is to be fasting for 1 hour prior to the test. No food, liquids, or smoking; Abstain from the following medications for 2 weeks prior to the test: all antibiotics, Proton Pump Inhibitors (Prilose, Prilosec OTC, Prevacid, Aciphex, Protonix, and Nexium), generic versions of PPIs and Bismuth preparations such as Pepto Bismol. If a patient is currently taking PPIs and the test is positive for H. pylori, it is considered positive and be acted upon. If it is negative for H. pylori while currently taking PPIs, it may be a false negative and the test should be repeated two weeks after discontinuing the PPI treatment. Patient can use Zantac, Tagamet, Pepcid, and Aixd.

**Collection Procedure:** Breath samples using Breath Tek UBT Kit-one blue bag for the baseline sample and one pink bag for the post dose sample. Follow instructions contained in the collection kit.

**Specimen Processing:** Complete required information and send both pink and blue bags at room temperature.

**Stability:** Room Temp 1 week.

**Unacceptable conditions:** Bags not fully inflated; samples with only one of the bags received; time between ingestion of Panactin-Citric solution and post-dose sample collection must be 15 to 20 minutes.

**SUPPLY ITEM NUMBER** 8058

**SCHEDULE** Mon. - Sat.

**TURNAROUND** 1 - 4 days

**RANGES** Helicobacter pylori Breath Test Negative

**NOTES** Determination of the eradication of Helicobacter pylori bacteria should be done at least 4 weeks after the completion of therapy.

For more information, please contact your local sales representative.
1 Intended Use

The BreathTek® UBT for H. pylori Kit (BreathTek UBT Kit) is intended for use in the qualitative detection of urease associated with H. pylori in the human stomach and is indicated as an aid in the initial diagnosis and post-treatment monitoring of H. pylori infection in adults, and pediatric patients 3 to 17 years old. The test may be used for monitoring therapy if used at least 4 weeks following completion of therapy. For these purposes, the system utilizes an Infrared Spectrophotometer for the measurement of the ratio of 13CO2 to 12CO2 in breath samples, in clinical laboratories and point-of-care settings. The Pediatric Urea Hydrolysis Rate Calculation Application (pUHR-CA), provided as a web-based calculation program, is required to obtain pediatric test results. The BreathTek UBT Kit is for administration by a healthcare professional, as ordered by a licensed health care practitioner.

2 Summary and Explanation

Since the isolation of the spiral urease-producing Helicobacter pylori (H. pylori) bacteria in 1983 by Drs. Marshall and Warren,1 a significant body of evidence has accumulated indicating that the bacteria is an important pathogen in the upper GI tract of humans. H. pylori is associated with a number of GI conditions including chronic gastritis, peptic ulcer disease, and gastric malignancy.2-4 Methods available for detecting current infection of the human stomach by H. pylori are generally divided into two (2) general types: Invasive and Non-invasive.

Invasive methods are so named because they include, as a first step, an esophagogastroduodenoscopy (“EGD”) with collection of gastric biopsies. These biopsies are then examined by one or more detection methods: histological examination of stained tissue, microbiological culture of the organism, or direct detection of urease activity in the tissue. Biochip based methods are expensive, entail some patient risk and discomfort and may give false negative results due to sampling errors when colonization of the gastric mucosa is patchy.5 Non-invasive methods include serological testing, fecal antigen test, and urea breath test. Several serological tests that detect serum antibodies to H. pylori are commercially available. A positive result with a serologic test cannot distinguish between current infection and past exposure to infection and, therefore, is not a conclusive indicator of current gastrointestinal colonization by H. pylori.

Urea breath tests are a non-invasive method for detecting current H. pylori infection.

3 Principle of the BreathTek UBT for H. pylori

3.1 Description of the Pranactin®-Citric Diagnostic Drug Component

The diagnostic drug component of the kit is 13C-urea, a synthetic urea contained in a granulated powder (Pranactin-Citric) for reconstitution with potable water to provide a clear solution for oral administration. The carbon in the drug component is predominantly Carbon-13, a stable, naturally occurring, non-radioactive isotope of carbon; the relative abundance of Carbon-13 is greater than or equal to 99%.

Each gram dose of Pranactin-Citric is supplied in a polyethylene-lined foil pouch and contains 75 mg of 13C-urea, citric acid, aspartame and mannitol. 13C-urea is the diamine of 14C-carboxylic acid and is highly soluble in water (1 gram per ml at 25°C). It has the following chemical formula: CH3N2O. An average adult body normally contains about 9 grams of urea, which is a product of protein metabolism. Urea in the body is referred to as natural isotopic abundance urea since it is measured in adults. It is known that the measured Delta over Baseline (DOB) is a function of the Pranactin®-Citric Diagnostic Drug Component.

3.2 Principle of the Test

Pranactin-Citric is a drug product that is a component of the BreathTek UBT Kit. Three (3) g of reconstituted Pranactin-Citric containing 75 mg of 13C-urea is ingested by the patient. In the presence of urease associated with gastric H. pylori, the 13C-urea ([NH3], 13CO2) is decomposed to 13CO2 and NH3, according to the following equation:

\[
\text{H. pylori urease} \quad (\text{NH}_3) + \text{CO}_2 + \text{H}_2 \text{O} \rightarrow \text{13CO}_2 + 2\text{NH}_2.
\]

The 13CO2 is absorbed in the blood, and then exhaled in the breath. It results in an increase in the ratio of 13CO2 to 12CO2 in a POST-DOSE breath sample taken after the Pranactin-Citric solution was consumed, compared to a BASELINE sample taken before the Pranactin-Citric solution was consumed. Analysis of the breath samples is performed by UBiT®-IR300 Infrared Spectrophotometer located at your clinical laboratory and point-of-care settings.

In the absence of gastric H. pylori, the 13C-urea does not produce 13CO2 in the stomach. The ratio of 13CO2 in the POST-DOSE breath sample remains essentially the same as the BASELINE.

3.3 Adjustment of Endogenous CO2 Production with UHR Calculation in Pediatric Patients

The measured difference between the ratios of 13CO2/12CO2 values before and after administration of Pranactin-Citric solution is referred to as Delta over Baseline (DOB). DOB is the primary outcome measure reported in pediatric patients. It is known that the measured Delta over Baseline (DOB) is a function of anthropometric variables, which determine the rate of CO2 production.6

While the effect of the CO2 production rate is small between adults, it can be significant in pediatric patients. Therefore, in performing the BreathTek UBT on pediatric patients, the primary outcome measure reported for the BreathTek UBT is the UHR. The UHR is calculated as shown below:

\[
\text{UHR (mg/ml)} = \text{DOB} \times \text{CO} \times \text{Production Rate} \times 0.3427
\]

4 Warnings and Precautions

4.1 For in vitro diagnostic use only. The Pranactin-Citric solution is taken orally as part of the diagnostic procedure.

4.2 Phenylketonurics: Contains Phenylalanine (one of the protein components of Aspartame), 84 mg per dosage unit. (For reference, 12 ounces of typical diet cola soft drinks contain approximately 80 mg of Phenylalanine.)

4.3 A negative result does not rule out the possibility of H. pylori infection. False negative results do occur with this procedure. If clinical signs are suggestive of H. pylori infection, refer to a new sample or an alternate method.

4.4 False negative test results may be caused by:

- Ingestion of proton pump inhibitors (PPIs) within 2 weeks prior to performing the BreathTek UBT. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to the BreathTek UBT, it may be a false negative result and the test should be repeated 2 weeks after discontinuing the PPI treatment. A positive result for a patient on a PPI could be considered positive and be acted upon.
- Ingestion of antibiotics, or bismuth preparations within 2 weeks prior to performing the BreathTek UBT
- Premature POST-DOSE breath collection time for a patient with a marginally positive BreathTek UBT result
- Post-treatment assessment with the BreathTek UBT less than 4 weeks after completion of treatment for the eradication of H. pylori.

4.5 False positive test results may be caused by:

- Urea associated with other gastric spiral organisms observed in humans such as Helicobacter heilmannii.
- Achlorhydria
- Oral contamination associated with urea containing bacteria especially when not using the straw provided in the BreathTek UBT kit.

4.6 If particulate matter is visible in the reconstituted Pranactin-Citric solution after thorough mixing, the solution should not be used.

4.7 Hypersensitivity: Patients who are hypersensitive to mannitol, citric acid or Aspartame should avoid taking the drug solution as this drug solution contains these ingredients. Swallowed lip and rash were reported in the pediatric clinical studies.

4.8 Risk of Aspiration: Use with caution in patients with difficulty swallowing or who may be at high risk for aspiration due to medical or physical conditions.

4.9 Pregnancy/Lactation: The safety of using the BreathTek UBT kit during pregnancy and lactation is not established.

4.10 For repeat test results, the UHR results must be calculated. DOB results in conjunction with Pediatric Urea Hydrolysis Rate Calculation Application (pUHR-CA), provided as a web-based calculation program, is required to obtain pediatric test results.

4.11 Safety and effectiveness has not been assessed in children below the age of 3 years.

5 Adverse Events

5.1 Adults-Postmarketing Experience

During post-approval use of the BreathTek UBT, the following adverse events have been identified: anaphylactic reaction, hypersensitivity, rash, burning sensation in the stomach, tingling in the skin, vomiting and diarrhea. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to establish a causal relationship to drug exposure.

5.2 Pediatrics-Clinical Experience

In two clinical studies conducted on 176 (analyzed) pediatric patients ages 3 to 17 years to determine the initial diagnosis and post-treatment monitoring of H. pylori infection, the following adverse events were experienced by ≥21% of these patients were: vomiting (5.1%), oropharyngeal pain (4.5% to 14.1%), abdominal pain (3.0%), diaphoresis (2.3%), and headache (1.1%). It is known that the measured Delta over Baseline (DOB) is a function of anthropometric variables, which determine the rate of CO2 production.

7.2 The patient should have fasted at least 1 hour before administering the BreathTek UBT.

7.3 The patient should not have taken antibiotics, proton pump inhibitors (PPIs), or bismuth preparations within 2 weeks prior to performing the BreathTek UBT. If PPIs are used within 2 weeks of BreathTek UBT testing, false negative test results may occur, and the test should be repeated 2 weeks after discontinuation of PPI treatment. A positive result for a patient on a PPI could be considered positive and be acted upon.

7.4 The effect of histamine 2-receptor antagonists (H2RAs) may reduce urease activity on urea breath tests. \(^{12}\) H2RAs may be discontinued for 24-48 hours before the BreathTek UBT.

7.5 Use of antacids does not appear to affect the accuracy of the BreathTek UBT.13

7.6 For administration by a healthcare professional only. Do not provide this kit to the patient for self-administration.

7.7 If repeat testing is needed, BreathTek UBT can be administered again on the following day.14

8 Procedure for Collecting Breath Samples Using BreathTek UBT Kit, for Analysis by Infrared Spectrophotometer

8.1 Materials

8.1.1 Materials provided

Each sealed single-patient BreathTek UBT Kit contains:

- One (1) sample transport bag
- Two (2) breath collection bags, one (1) blue bag for the BASELINE sample and one (1) pink bag for the POST-DOSE sample.
- Test instructions
- One (1) pouch of Pranactin-Citric powder (3 g)
- A set of four (4) self-adhesive bar-code stickers. All bar-codes should bear the same number.
- Two (2) breath collection bags, one (1) blue bag for the BASELINE sample and one (1) pink bag for the POST-DOSE sample.
- One (1) sample transport bag

BreathTek® UBT for H. pylori Kit
8.1.2 Materials needed but not provided

- One (1) plastic straw
- One (1) plastic drinking cup

8.1.3 Instruments and Software

- In adult patients, an Infrared Spectrophotometer (UBiT-IR300 or POClone, Otsuka Pharmaceutical Co., Ltd.) is required for analysis of breath samples.
- In pediatric patients,
  - Use the UBiT-IR300 or POClone Infrared Spectrophotometer to analyze the breath samples.
  - Use of the Pediatric Urea Hydrolysis Rate Calculation Application (pUHR-CA), as a web-based calculation program, is required to obtain the test result.

8.2 Step-By-Step Procedure

Time intervals listed in the following step-by-step procedure are critical. They are highlighted by the timer icon:

8.2.1 Verify that the patient has been prepared for the test as specified in Section 7.

8.2.2 Open the BreathTek UBT Kit, which should contain all the materials listed in Step 8.1.1. Label each breath collection bag to maintain patient identification using the bar-code labels provided, or according to your laboratory or office procedure.

8.2.3 Collect the BASELINE breath sample according to the following procedure:

a. Pick up the blue breath collection bag.

b. Remove the pull-off cap from the mouthpiece of the breath collection bag.

c. Instruct the patient to (1) breathe normally; (2) take a deep breath then pause momentarily; (3) exhale into the mouthpiece of the bag.

d. Replace the cap firmly until it clicks on the mouthpiece of the bag.

8.2.4 Prepare the Pranactin-Citric solution no more than 60 minutes before administering it to the patient. Urea slowly decomposes in water.

a. Pick up the Pranactin-Citric pouch. Tap the upright packet of Pranactin-Citric to settle the contents in the bottom half.

b. Tear off the top of the packet and carefully empty the contents into the drinking cup provided, making sure to transfer all of the contents by tapping on the bottom of the pouch.

c. Add drinking water to the fill line indicated on the outside of the cup by a raised plastic ridge.

d. Close the lid securely by pressing down until you hear a click and swirl the mixture for up to 2 minutes to dissolve the packet contents; typically, only 1 minute is required for complete dissolution. The resulting drug solution should be clear with no particulate matter. If particulate matter is present after thorough mixing, the drug solution should not be used.

8.2.5 Instruct the patient, including pediatric patients aged 3-17 regardless of age and body weight, to drink all of the drug solution with the straw provided, without stopping. Advise the patient NOT to rinse the inside of his/her mouth with the drug solution before swallowing.

a. Discard the straw after the patient has finished drinking the drug solution.

b. Not using the straw may result in inaccurate results.

8.2.6 Set the timer for 15 minutes. The patient should sit quietly and should not eat, drink or smoke during the 15 minute interval. Breath sample may be collected no later than 30 minutes POST-DOSE.

8.2.7 After 15 minutes have elapsed, pick up the pink breath collection bag. Collect the POST-DOSE breath sample according to the procedure described in Steps 8.2.3 b through 8.2.3 d.

8.2.8 Store the specimens at 15°-30°C (59°-86°F) until analysis is performed.

8.2.9 Perform breath sample analysis within 7 days of breath sample collection. If desired, use the web-based pUHR-CA to calculate the UHR and obtain pediatric test results.

8.2.10 When shipping breath sample bags from pediatric patients to a laboratory for analysis, no more than 60 minutes before administering it to the patient. Urea slowly decomposes in water.

9 Quality Control

Complete operating information, including self-diagnostic instrument routines and user maintenance procedures provided in the Instruction Manuals for the UBT-IR300 Spectrophotometer, the UBT-AS10 Autosampler, the POCone Infrared Spectrophotometer and the POClone-Citric solution, respectively. Additionally, each office laboratory or test facility should follow its own internal procedures for quality control.

10 Test Results

10.1 Adults

10.1.1 The Test Method

The ratio of 14CO2 to 13CO2 in breath samples is determined by Infrared Spectrophotometer, either UBT-IR300 or POClone.

10.1.2 Calculation of Results

The result is provided as the Delta over Baseline (DOB) which is the difference between the ratio of 14CO2/13CO2 in the POST-DOSE sample and the corresponding ratio in the BASELINE sample.

No calculations are required by the user.

10.1.3 Determination of the Cut-off Point

The DOB cutoff value is 2.4 as determined in a controlled study of 66 infected and 53 uninfected asymptomatic, apparently healthy volunteers. Histological examination of biopsy tissue was used as the reference standard.

Meretek UBT™

Meretek UBT is an earlier version of the BreathTek UBT. The drug component of the test contained 125 mg of "C-urea. Analysis of the breath samples was performed by gas isotope ratio mass spectrometry (GRMS). DOB values for the Meretek UBT were determined in a controlled clinical study of 66 infected and 53 uninfected asymptomatic, apparently healthy volunteers. Histological examination of biopsy tissue was used as the reference method in the determination of infection in this study. The Meretek UBT DOB values for the uninfected group ranged from 0.0 to 2.2. The DOB cutoff value for Meretek UBT was determined to be 2.4 in this study. Distribution of Meretek UBT DOB values in infected and uninfected groups in this study is shown in Figure 1a. The Meretek UBT was subsequently validated in clinical trials of patients with documented duodenal ulcer disease (see Section 13.4).

BreathTek UBT

For the BreathTek UBT, the DOB cutoff values was determined to be 2.4 in a controlled study of 26 infected and 23 uninfected adult volunteers. Test subjects were judged to be in acceptable health based on the results of a medical history and physical examination and demonstrated no uncontrolled clinically significant abnormality other than, for some, symptoms of peptic ulcer. The Meretek UBT was used as the reference standard. The range of BreathTek UBT DOB values for the uninfected group was determined to be 0.0 to 1.0. The cutoff value was calculated by determining the BreathTek UBT result level at which negative and positive subjects were best distinguished by co-optimization of relative sensitivity and specificity. Distribution of BreathTek UBT DOB values in infected and uninfected groups in this study is shown in Figure 1b.

The 2.4 cutoff point for the BreathTek UBT was validated in an independent study by retrospective analysis of Clinical Field Trial data collected on 145 H. pylori negative and 105 H. pylori positive test subjects using the original Meretek UBT as a reference (see Section 13.4.2).

10.2 Pediatrics

10.2.1 The Test Method

The ratio of 14CO2 to 13CO2, in breath samples from children aged 3 - 17 years is determined by the UBT-IR300 or POClone Infrared Spectrophotometer. Although the DOB result of the BreathTek UBT is provided by the UBT-IR300 or POClone Infrared Spectrophotometer, urea hydrolysis rate (UHR) using the pUHR-CA, a web-based calculation program, is required to obtain the test results in pediatric patients.

10.2.2 Calculation of Results

The web-based pUHR-CA converts DOB to the UHR result in pediatric patients. The calculation incorporates the patient's anthropometric data (i.e., age, gender, height, and body weight) to calculate the CO2 production rate in that patient. The UHR is calculated as shown below:

\[ \text{UHR (µg/min)} = \text{DOB} \times \text{CO}_2 \times \text{Production Rate} \times 0.3427 \]

10.2.3 Determination of the Cutoff Point

UHR values from pediatric patients were first determined in a group of 312 asymptomatic preschool and school-age children aged 1 - 10 years in the Houston, Texas, area. An UHR cut-off value was determined to be 10.0 µg/min.

This UHR cut-off value was subsequently validated in two multi-center, controlled clinical studies of dyspeptic children aged 3 - 17 years using the BreathTek UBT kit and the UBT-IR300 Infrared Spectrophotometer (see Section 13.5 for more information). H. pylori infection was established with an endoscopic composite reference method criteria consistent with the FDA guidance. Of the 176 analyzed study subjects, the range of UHR values were 0.0 - 10.9 µg/min for the 128 uninfected children and 3.4 - 403.8 µg/min for the 48 infected children. Distribution of the UHR values is shown in Figure 2. Note that the UHR scale is logarithmic; therefore, in displaying negative UHR values on a logarithmic scale, value between -5 and 0 were assigned a value of 0.01.

Figure 2: Data Distribution and Cutoff for UHR

10.2.4 Interpretation of Results for Pediatrics

A UHR value of ≥ 2.4 µg/min is interpreted as diagnostically positive indicating the presence of urease associated with H. pylori. A UHR value of < 2.4 µg/min is interpreted as diagnostically negative indicating the absence of urease associated with H. pylori. The same DOB cutoff value applies to both initial diagnosis and post-treatment monitoring of H. pylori infection. The infrared Spectrophotometer applies to both initial diagnosis and post-treatment monitoring of H. pylori infection in children.
11 Limitations of the Test

11.1 The BreathTek UBT should not be used until 4 weeks or more after end of treatment for eradication of H. pylori as earlier post-treatment assessment may give false negative results.

11.2 The performance characteristics for initial diagnosis and post-treatment monitoring for pediatric patients < 3 years of age have not been established for this test.

11.3 The specimen integrity of breath samples and reference gases stored in breath bags under ambient conditions has not been determined beyond 7 days.

11.4 A correlation between the number of H. pylori organisms in the stomach and the BreathTek UBT result has not been established.

11.5 Do not use DOB to determine the H. pylori positive or negative results in pediatric patients. Use the web-based pHUHR-CA to calculate the UHR to obtain pediatric test results.


11.6 The web-based pHUHR-CA to calculate the UHR to obtain pediatric test has only been tested with Firefox and Internet Explorer.

12 Expected Values

12.1 Adults

DOB values for the BreathTek UBT were determined in a controlled clinical study of 26 infected and 23 uninfected adult volunteers. The Meretek UBT, an earlier version of the BreathTek UBT, was used as the reference method in the diagnosis of infection. The range of BreathTek UBT DOB values for the uninfected group was determined to be 0.0 to 1.0 (see Figure 1b).

12.2 Pediatrics

Of the 176 analyzed study subjects described in Section 10.2, the range of UHR values were 0.0 - 10.9 μg/min for the uninfected children and 3.4 - 403.8 μg/min for the infected children (see Figure 2).

13 Performance Characteristics

13.1 The primary performance measure for clinical validation of both the Meretek UBT and the BreathTek UBT is a composite reference method consisting of histology and H. pylori culture of endoscopically-obtained gastric biopsies as well as a urease detection assay.10,11

13.2 Analytical Performance Characteristics for the UBT-IR300 Infrared Spectrophotometer. Refer to the Instruction Manual for the instrument.

13.3 Analytical Performance Characteristics for the POCone Infrared Spectrophotometer. Refer to the Instruction Manual for the instrument.

13.4 Clinical Performance in Clinical Trials for Adults

13.4.1 Comparison of Meretek UBT with the Composite Reference Method in the Adult Population

a. Experimental Design

The clinical performance data presented here were collected from a prospective, cross-over clinical field trial designed to validate the BreathTek UBT test procedure and to examine the effect of pre-test fasting time on test performance. The study included 252 adult test subjects from Houston and Galveston, Texas. Subjects were judged to be in acceptable health based on the results of a medical history and physical examination and demonstrated no uncontrolled clinically significant abnormality other than, for some, symptoms of dyspepsia. Test subjects were tested for H. pylori infection using the Meretek UBT according to established procedure and with the BreathTek UBT under differing conditions of pre-test fasting times. Otherwise, no special instructions were given to subjects beyond those listed in the step-by-step procedures for administration of the Meretek UBT Breath Test and BreathTek UBT. To minimize potential bias due to test order, the sequence of urea breath tests administered to each subject was randomized. All breath tests were administered to a given individual within 14 days of one another, most often and at a minimum, on successive days.

b. Results

It was demonstrated in the field trial that the BreathTek UBT may be administered at any time beyond 1 hour after consuming solid and/or liquid food.

Point estimates of Percent Agreement of the BreathTek UBT with Meretek UBT positive and negative results are listed in the contingency table (Table 3). The comparative method for determining the true diagnosis was the predicate device (Meretek UBT) rather than endoscopic methods. The exact binomial distribution was used to calculate the lower and upper limits of the 95% confidence intervals of the performance statistics. The confidence intervals are entered in parentheses following the point estimate of the statistic.

Table 3. Comparison of BreathTek UBT (2-hour fast) with Meretek UBT

| BreathTek UBT Results | Meretek UBT Results | Percent Agreement with Meretek UBT positive subjects: 99.1% [95% CI: (94.9, 100.0)]
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Percent Agreement with Meretek UBT positive subjects: 99.1% [95% CI: (94.9, 100.0)]
Percent Agreement with Meretek UBT negative subjects: 99.3% [95% CI: (96.2, 100.0)]

13.4.2 Comparison of the BreathTek UBT with the Meretek UBT in the Adult Population

The clinical performance data presented here were collected from a prospective, cross-over clinical field trial designed to validate the BreathTek UBT test procedure and to examine the effect of pre-test fasting time on test performance. The study included 252 adult test subjects from Houston and Galveston, Texas. Subjects were judged to be in acceptable health based on the results of a medical history and physical examination and demonstrated no uncontrolled clinically significant abnormality other than, for some, symptoms of dyspepsia. Test subjects were tested for H. pylori infection using the Meretek UBT according to established procedure and with the BreathTek UBT under differing conditions of pre-test fasting times. Otherwise, no special instructions were given to subjects beyond those listed in the step-by-step procedures for administration of the Meretek UBT Breath Test and BreathTek UBT. To minimize potential bias due to test order, the sequence of urea breath tests administered to each subject was randomized. All breath tests were administered to a given individual within 14 days of one another, most often and at a minimum, on successive days.

b. Results

It was demonstrated in the field trial that the BreathTek UBT may be administered at any time beyond 1 hour after consuming solid and/or liquid food.

Point estimates of Percent Agreement of the BreathTek UBT with Meretek UBT positive and negative results are listed in the contingency table (Table 3). The comparative method for determining the true diagnosis was the predicate device (Meretek UBT) rather than endoscopic methods. The exact binomial distribution was used to calculate the lower and upper limits of the 95% confidence intervals of the performance statistics. The confidence intervals are entered in parentheses following the point estimate of the statistic.

Table 4. Agreement of UBT-IR300 and GIRMS for 13C urea breath test

<table>
<thead>
<tr>
<th>GIRMS Results</th>
<th>UBT-IR300 Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>115</td>
</tr>
<tr>
<td>Negative</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>117</td>
</tr>
</tbody>
</table>

Percent Overall Agreement: 99.06% [95% CI: (97.28, 99.97)]
Percent Positive Agreement: 98.29% [95% CI: (94.26, 99.70)]
Percent Negative Agreement: 99.5% [95% CI: (99.43, 99.97)]

13.4.3 Comparison of Gas Isotope Ratio Mass Spectrometry (GIRMS) and UBT-IR300 Infrared Spectrophotometry Method in the Adult Population

A multi-center prospective clinical trial was conducted to compare the UBT-IR300 method with the traditional GIRMS method. The study included a total of 320 adult test subjects enrolled at 4 physicians’ office laboratory (POL) settings and at a clinical laboratory. The results of the clinical trial are provided in the Instructional Manual for the UBT-IR300 Infrared Spectrophotometer (refer to the Application Note, 13C-Urea Breath Test using the UBT-IR300 Infrared Spectrophotometry System).

Table 4 shows the percent agreement of the UBT-IR300 results as compared to the GIRMS method. Overall agreement was excellent at 99.06 percent.

Table 4. Agreement of UBT-IR300 and GIRMS for 13C urea breath test

<table>
<thead>
<tr>
<th>GIRMS Results</th>
<th>UBT-IR300 Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>115</td>
</tr>
<tr>
<td>Negative</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>117</td>
</tr>
</tbody>
</table>

Percent Overall Agreement: 99.06% [95% CI: (97.35, 99.74)]
Percent Positive Agreement: 98.29% [95% CI: (94.26, 99.70)]
Percent Negative Agreement: 99.5% [95% CI: (99.43, 99.97)]

13.4.4 Comparison of UBT-IR300 and POCone Infrared Spectrophotometry Methods in the Adult Population

A multi-center, prospective study was conducted to compare the POgone Infrared Spectrophotometer to the UBT-IR300 Infrared Spectrophotometer for measuring 13CO2 enrichment in breath. The study included a total of 220 adult test subjects enrolled at 5 physicians’ office laboratory (POL) and point of care (POC) settings. The results of the clinical trial are provided in the Instruction Manual for the POgone Infrared Spectrophotometer (refer to the Application Note, 13C-Urea Breath Test using the POgone Infrared Spectrophotometry System).
Table 5 shows the percent agreement of the POC-one results with the UBT-IR300 results. Overall agreement was 99.55 percent.

| Table 5. Agreement of POCone and UBT-IR300 for the 13C urea breath test |
|-------------------------|-------------------------|
| **UBT-IR300 Results**  | **POCone Results**     |
| **Positive** Positive  | 86                      |
|                       Negative | 1                       |
| **Total**             | 87                      |
|                       Negative | 133                     |
| **Total**             | 134                     |
|                       133                     |
|                       220                     |

Percent Overall Agreement: 99.55% [95% CI: (97.67, 99.98)]
Percent Positive Agreement: 100.00% [95% CI: (95.90, 100.00)]
Percent Negative Agreement: 99.25% [95% CI: (96.27, 99.96)]

13.5 Clinical Performance in Clinical Trials for Pediatric Patients

a. Experimental Design

The clinical performance data were collected from a multi-center, open-label study designed to compare the BreathTek UBT with endoscopic methods for the initial diagnosis of H. pylori in pediatric population. Subjects were symptomatic pediatric patients 3 to 17 years old undergoing diagnostic upper endoscopy at the determination of their treating pediatric gastroenterologist. Study enrollment was based on esophagogastroduodenoscopy (EGD) performed on each subject in proximity to the administration of the BreathTek UBT test.

The study enrolled 206 pediatric patients at five (5) U.S. investigational sites (New Orleans, Louisiana, Miami, Florida, Houston, Texas, Huntington, West Virginia and Detroit, Michigan) of which 176 subjects were evaluated for analysis.

b. Results - Comparison of BreathTek UBT UHR to the Composite Reference Method Criteria

The primary endpoint analysis was conducted to determine the sensitivity and specificity of the BreathTek UBT UHR to the composite reference method criteria for the 176 evaluable cases. Table 6 demonstrates the diagnostic performance of the BreathTek UBT (expressed as UHR) compared to the composite reference method criteria in pediatric patients aged 3-17 years old.

Table 6. Comparison of Composite Reference Method Criteria and BreathTek UBT (UHR) in Pediatric Patients for Initial Diagnosis

<table>
<thead>
<tr>
<th>Age Group</th>
<th>UBT-IR300 UHR</th>
<th>POCone UHR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-5 Years</td>
<td>Sensitivity</td>
<td>100.0</td>
</tr>
<tr>
<td>6-12 Years</td>
<td>Specificity</td>
<td>95.8</td>
</tr>
<tr>
<td>13-18 Years</td>
<td>Sensitivity</td>
<td>95.8</td>
</tr>
<tr>
<td>All Age Groups Combined</td>
<td>Specificity</td>
<td>95.8</td>
</tr>
</tbody>
</table>

The agreement was 99.55 percent for the 13C urea breath test.

13.5.3 Comparison of UBT-IR300 and POCone Infrared Spectrophotometry Methods in the Pediatric Population

a. Experimental Design

A multi-center, prospective study was conducted to compare the POCone to the UBT-IR300 in measuring 13CO2/12CO2 ratio in breath samples when used together with the BreathTek UBT Kit and the pH UHR-CA in identifying H. pylori infection in pediatric subjects. The study included a total of 99 pediatric subjects ages 3 – 17 years enrolled at two pediatric gastroenterology clinics and one general pediatric clinic. The breath samples were analyzed and UHR calculated either at the point-of-care setting or at a central laboratory. Twenty (20) subjects who tested positive at the initial visit returned for post-treatment monitoring test 4 weeks or longer after a course of H. pylori eradication therapy.

b. Results – Comparison of the POCone (UHR) to the UBT-IR300 (UHR)

Table 8 shows the percent agreement of the POCone results with the UBT-IR300 results in 95 evaluable cases as part of the initial diagnosis. Overall agreement was 100 percent.

Table 8. Agreement of POCone and UBT-IR300 for the BreathTek UBT When Used Together with the pH UHR-CA

<table>
<thead>
<tr>
<th>UBT-IR300 UHR</th>
<th>POCone UHR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>24</td>
</tr>
<tr>
<td>Negative</td>
<td>71</td>
</tr>
<tr>
<td>Total</td>
<td>95</td>
</tr>
</tbody>
</table>

Percent Overall Agreement: 100% [95% CI: (96.2, 100.0)]
Percent Positive Agreement: 100% [95% CI: (95.5, 100.0)]
Percent Negative Agreement: 100% [95% CI: (94.9, 100.0)]

The agreement was also 100 percent in the 19 evaluable cases as part of the post-treatment monitoring. Nine (9) cases tested positive and 10 case negative by both instruments.

14 Bibliography


15 Name and Place of Business

The BreathTek UBT for H. pylori Kit is manufactured for Medical Device Division of Otsuka America Pharmaceutical, Inc., 2440 Research Boulevard, Rockville, MD 20850. For additional information, please call 1 888.637.3853 or visit www.BreathTek.com.
What is BreathTek UBT?

The BreathTek UBT Kit is intended for use in the qualitative detection of urease associated with H. pylori. The test may be used for monitoring treatment if used at least 4 weeks following completion of PPI therapy for H. pylori infection. For these purposes, the system utilizes an Infrared Spectrophotometer for the measurement of the ratio of 13CO2 to 12CO2 in breath.

TEST, TREAT, CONFIRM

Test:

- Diagnostic if H. pylori is the underlying issue.
- Confirm if recommended by OSHA or IDSA recommendations for patients who test positive.

Treat: 4 weeks after the end of treatment to allow time for adequate resolution if indications are unsatisfactory.

For more information, please visit www.BreathTek.com or call 888-637-3835.

Please see accompanying BRIEF SUMMARY and enclosed Current Package Insert.
ICD-10 Coding Guide

Partial list: Please contact individual plans for a list of codes that support medical necessity.

The BreathTek UBT Kit is for administration by a health care professional, as ordered by a licensed health care practitioner. Please see accompanying BRIEF SUMMARY and enclosed Current Package Insert.

For more information, please visit www.BreathTek.com, or call 888-637-3835.

Confirm:
• Test. Treat. Confirm.

The BreathTek UBT Kit is intended for use in the qualitative detection of urease associated with Helicobacter pylori in the human stomach and as an aid in monitoring treatment if used at least 4 weeks following completion of therapy. For these purposes, the system utilizes an Infrared detection system that elicits a Quantitative test response to urease activity

What is BreathTek UBT?

Helicobacter pylori

Stomach

The BreathTek UBT Kit is for administration by a health care professional, as ordered by a licensed health care practitioner.

Drug administration and sample collection

Ingestion of pranactin citrate tablets should be performed at least 1 hour after meals. The BreathTek UBT Kit cannot be used to determine the infection status in pediatric patients. DOB results may be caused by urease associated with other gastric spiral organisms observed in humans such as H. heilmannii or achlorhydria.

Pretest conditions

Ingestion of proton pump inhibitors (PPIs) within 2 weeks prior to performing the BreathTek UBT could cause a false-negative result. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to performing the BreathTek UBT, retest with a new sample or an alternate method.

PPI treatment should be withheld for at least 2 weeks following discontinuation of any PPI therapy prior to performing the BreathTek UBT.

Post-traitment assessment with the BreathTek UBT test less than 4 weeks after completion of treatment for the eradication of H. pylori.

False positive test results may be caused by urease associated with other gastric spiral organisms observed in humans such as H. heilmannii or achlorhydria.

Long-term treatment with proton pump inhibitors (PPIs) has been shown to increase the risk of developing Helicobacter pylori infection. False negative results do occur with this procedure. If clinical signs and symptoms of Helicobacter pylori infection, retest with a new sample or an alternate method.

Bacterial overgrowth or other gastric conditions such as the presence of Helicobacter heilmannii or Helicobacter heilmannii or other gastrointestinal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma] cannot be used to determine the infection status in pediatric patients. Use the web-based pPhCA (https://BreathTek.com) to calculate the UHR.

Safety and effectiveness has not been established in children below the age of 3 years.

Adverse Events

During post-approval use of the BreathTek UBT in adults, the following adverse events have been identified: aberrant mood, sleep disturbances, tingling in the hands and feet, burning sensation in the stomach, tingling in the skin, rash, nausea, vomiting, headache, hypertension, constipation, diarrhea, flatulence, abdominal pain, abdominal distention, and anaphylaxis.

Children ages 3 to 17 years were observed among the 99 subjects enrolled: 2 incidences of headache, and 1 incidence each of cough, dry mouth and acute upper respiratory infection.

In two clinical studies conducted in 176 (analyzed) pediatric patients ages 3 to 17 years to determine the initial diagnosis and post treatment monitoring of H. pylori, the following adverse events experienced by 1% of these patients were: vomiting (2.3%), epistaxis permitted 6.5% to include throat irritation, sore throat, throat burning), nausea (2.3%), vomiting (2.3%), sore throat(s) ulcerated (1.1%) and diarrhea (1.1%). Most of these events were transient and mild and resolved after the medication was discontinued. Adverse reactions for patients within minutes to hours of ingestion of the PPI therapy drug. In another clinical study comparing the UBT® and POCon® in pediatric patients ages 3 to 17 years, the following adverse events were observed: 3 (3.3%) in the UBT® group and 99 (99%) subjects enrolled: 2 incidences of headache, and 1 incidence each of cough, dry mouth and acute upper respiratory infection.

Please see accompanying Current Package Insert.

References

The guidelines make it clear...

Use a test for active infection to detect *H. pylori* and confirm eradication.\(^1\)\(^2\)
Brief Summary about BreathTek UBT

Intended Use
The BreathTek UBT for H. pylori Kit (BreathTek UBT Kit) is intended for use in the qualitative detection of urease associated with H. pylori in the human stomach and is indicated as an aid in the initial diagnosis and post-treatment monitoring of H. pylori infection in adult patients and pediatric patients 3 to 17 years old. The test may be used for monitoring the treatment of the infection for at least 4 weeks following completion of therapy. The BreathTek UBT Kit utilizes an infrared Spectrophotometer for the measurement of the ratio of $\text{CO}_2$ to $\text{CO}_3$ breath samples, in clinical laboratories or point-of-care settings. The Pediatric Urea Hydrolysis Rate Calculation Application (pUHR-CA), provided as a web-based calculation program, is required to obtain pediatric test results.

The BreathTek UBT Kit is for administration by a health care professional, as ordered by a licensed health care practitioner.

Warnings and Precautions
- For in vitro diagnostic use only. The Pranactin®-Citric solution is taken orally as part of the diagnostic procedure and contains Phenylalanine (one of the protein components of Aspartame), 84 mg per dosage unit. (For reference, 12 ounces of typical diet cola soft drinks contain approximately 80 mg of Phenylalanine.)
- A negative result does not rule out the possibility of H. pylori infection. False negative results do occur with this procedure. If clinical signs are suggestive of H. pylori infection, repeat with a new sample or an alternate method.
- False positive test results may be caused by:
  - Ingestion of proton pump inhibitors (PPIs) within 2 weeks prior to performing the BreathTek UBT. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to the BreathTek UBT, it may be a false-negative result and the test should be repeated 2 weeks after discontinuing the PPI treatment. A positive result for a patient on a PPI could be considered positive and be acted upon.
  - Ingestion of antibiotics, or bismuth preparations within 2 weeks prior to performing the BreathTek UBT.
  - Premature POST-DOSE breath collection time for a patient with a marginally positive BreathTek UBT result.
  - Post-treatment assessment with the BreathTek UBT less than 4 weeks after completion of treatment for the eradication of H. pylori.
- False positive test results may be caused by:
  - Use associated with other gastric spiral organisms observed in humans such as Helicobacter heilmannii or achlorhydria.
  - Oral contamination associated with urease containing bacteria especially when not using the straw provided in the BreathTek UBT Kit.

Adverse Reactions During post-approval use of the BreathTek UBT in adults, the following adverse events have been identified: anaphylactic reaction, hypersensitivity, rash, burning sensation in the stomach, tingling in the skin, vomiting and diarrhea. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to establish a causal relationship to drug exposure.
In two clinical studies conducted in 176 (analyzed) pediatric patients ages 3 to 17 years to determine the initial diagnosis and post treatment monitoring of H. pylori, the following adverse events experienced by ≥1% of these patients were: vomiting (5.1%), oropharyngeal pain (4.5% to include throat irritation, sore throat, throat burning), rash (2.3%), restlessness (2.3%), stomach ache/belly pain (1.5%), and diarrhea (1.1%). Most of the adverse events were experienced by patients within minutes to hours of ingestion of the Pranactin-Citric solution.

Adverse Events

During post-approval use of the BreathTek UBT Kit in adults, the following adverse events have been identified: anaphylactic reaction, hypersensitivity, rash, burning sensation in the stomach, tingling in the skin, vomiting and diarrhea. These adverse events are reported voluntarily from a population of uncertain size, it is not always possible to establish a causal relationship to drug exposure.

In two clinical studies conducted in 176 (analyzed) pediatric patients ages 3 to 17 years to determine the initial diagnosis and post treatment monitoring of H. pylori, the following adverse events experienced by ≥1% of these patients were: vomiting (5.1%), oropharyngeal pain (4.5% to include throat irritation, sore throat, throat burning), nausea (2.3%), restlessness (2.3%), stomach ache/belly pain (1.5%), and diarrhea (1.1%). Most of the adverse events were experienced by patients within minutes to hours of ingestion of the Pranactin-Citric solution.

In another clinical study comparing the UBiT®-IR300 and POCone® in pediatric patients ages 3 to 17 years, the following adverse events were experienced by ≥1% of these patients were: vomiting (5.1%), oropharyngeal pain (4.5% to include throat irritation, sore throat, throat burning), nausea (2.3%), restlessness (2.3%), stomachache/belly pain (1.5%), and diarrhea (1.1%).

Most of the adverse events were experienced by patients within minutes to hours of ingestion of the Pranactin-Citric solution.

References:

January 2016 05US16IBR0001
Test, treat, confirm using BreathTek® UBT for H. pylori

The UBT method is a clear fit for a guideline-recommended strategy

- Guidelines recommend a test-and-treat strategy using noninvasive methods, such as UBT, for testing adults with uninvestigated dyspepsia1,2
- UBT is also recommended to confirm eradication in adults3,4 and children5

BreathTek UBT—approved as an aid in the initial diagnosis and post-treatment monitoring of H. pylori infection in adults and children ages 3 to 17 years

Please see accompanying BRIEF SUMMARY and enclosed Current Package Insert.

Learn more at BreathTek.com or call 888.637.3835.


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For diagnostic use only. The Pranactin®-Citric solution is taken orally as part of the diagnostic procedure. The BreathTek UBT Kit (BreathTek UBT Kit) is intended for use in the qualitative detection of urease associated with Helicobacter pylori in the human stomach and is indicated as an aid in the initial diagnosis and post-treatment monitoring of H. pylori infection in adult patients and pediatric patients 3 to 17 years old. The test may be used for diagnostic and post-treatment monitoring of H. pylori infection in adults and children ages 3 to 17 years. The BreathTek UBT Kit is for administration by a health care professional, as ordered by a licensed health care provider, in clinical laboratories or point-of-care settings. The Pediatric Urea Hydrolysis Rate Calculation Application (P-CA), provided as a web-based calculation program, is required to obtain pediatric test results.

Contraindications

- The safety of using the BreathTek UBT Kit during pregnancy and lactation is not established.
- Patients who are hypersensitive to mannitol, citric acid or Aspartame should avoid taking the drug solution as this may cause an allergic reaction. Hypersensitivity, rash, burning sensation in the stomach, tingling in the skin, vomiting and diarrhea may occur.
- False positive test results may be caused by:
  - Urease associated with other gastric spiral organisms observed in humans such as Helicobacter heilmannii or H. pylori
  - Post-treatment assessment with the BreathTek UBT less than 4 weeks after completion of treatment for the eradication of H. pylori
  - Premature POST-DOSE breath collection time for a patient with a marginally positive BreathTek UBT result.
  - Ingestion of antibiotics, or bismuth preparations within 2 weeks prior to performing the BreathTek UBT.
  - Ingestion of proton pump inhibitors (PPIs) within 2 weeks prior to performing the BreathTek UBT. If a negative result and the test should be repeated 2 weeks after discontinuing the PPI treatment. A positive result for a patient on a PPI could be considered positive and be acted upon.
  - Ingestion of achlorhydria.
  - False positive test results may also be caused by a high risk of aspiration due to medical or physical conditions.

Warnings and Precautions

- False positive test results may also be caused by some conditions that can cause a high risk of aspiration due to medical or physical conditions.
- False positive test results may also be caused by some conditions that can cause a high risk of aspiration due to medical or physical conditions.
- False positive test results may also be caused by some conditions that can cause a high risk of aspiration due to medical or physical conditions.

- The BreathTek UBT Kit is for administration by a health care professional, as ordered by a licensed health care provider, in clinical laboratories or point-of-care settings. The Pediatric Urea Hydrolysis Rate Calculation Application (P-CA), provided as a web-based calculation program, is required to obtain pediatric test results.
- False positive test results may also be caused by some conditions that can cause a high risk of aspiration due to medical or physical conditions.
- False positive test results may also be caused by some conditions that can cause a high risk of aspiration due to medical or physical conditions.
- False positive test results may also be caused by some conditions that can cause a high risk of aspiration due to medical or physical conditions.
You suspect *H. pylori*

**Now Confirm It**

Order a proven test for active infection

BreathTek® UBT or HpSA® Stool
Before you treat the symptoms, find the cause.

Why does the AGA* now recommend testing for *H. pylori* prior to prescribing PPIs?

- Successful eradication of *H. pylori* cures ulcer disease in 95% of cases.
- *H. pylori* is a class-one carcinogen that greatly increases the risk of gastric cancer.
- Following the AGA recommendation highlighted in Figure 1 will also reduce the overall cost of managing dyspepsia by reducing the costs associated with inappropriately prescribed Rx medication — particularly PPIs prescribed to suppress symptoms rather than treating the underlying cause.

Use a Test-Treat-Confirm Approach\(^1-3\)

**Test** to detect whether *H. pylori* is the underlying cause of the condition

**Treat** the patient if infection is detected

**Confirm** eradication at least 4 weeks after the end of treatment

*The "Test and Treat" strategy is recommended for adults with uninvestigated dyspepsia who are under the age of 55 years and have no alarm features.*\(^1\)

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\(^1\)American Gastroenterological Association

\(^2\)American College of Gastroenterology

\(^3\)American Society for Gastrointestinal Endoscopy

\(\)Cancer Research UK

\(\)European Foundation for the Study of Ulcer

\(\)Gastroenterological Society of Australia

\(\)Gastroenterological Society of New Zealand

\(\)Gastroenterological Society of Singapore

\(\)Gastroenterological Society of Thailand

\(\)Gastroenterological Society of Vietnam

\(\)Gastroenterological Society of Malaysia

\(\)Gastroenterological Society of Indonesia

\(\)Gastroenterological Society of the Philippines

\(\)Gastroenterological Society of the Republic of Korea

\(\)Gastroenterological Society of Japan

\(\)Gastroenterological Society of Korea

\(\)Gastroenterological Society of New Zealand

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\(\)Gastroenterological Society of the Philippines

\(\)Gastroenterological Society of the Republic of Korea

\(\)Gastroenterological Society of Japan

\(\)Gastroenterological Society of Korea

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**Management of Dyspepsia based on age and alarm features**

- **Age >55 or alarm symptoms**
  - **Positive**
    - Test for *H. pylori*
    - PPI trial 4-6 weeks
    - Reassurance, reassess diagnosis
  - **Negative**
    - EGD
    - PPI trial 4-6 weeks
    - Fails
    - Reassurance, reassess diagnosis
    - Consider EGD

- **Age <55 no alarm symptoms**
  - **Positive**
    - Treat for *H. pylori*
    - PPI trial 4 weeks
    - Fails
    - PPI trial 4 weeks
    - Fails
    - Consider EGD
  - **Negative**
    - EGD
    - PPI trial 4 weeks
    - Fails
    - PPI trial 4 weeks
    - Fails
    - Reassurance, reassess diagnosis
    - Consider EGD

**Notes:**
- *Bleeding, anemia, early satiety, unexplained weight loss, progressive dysphagia, odynophagia, recurrent vomiting, family history of GI cancer, previous esophagogastric malignancy*
Serology testing just isn’t good enough.

“Because of its lower specificity, serologic testing leads to more treatment of patients without active infection, more antibiotic resistance, and wasting of resources.”³

Both ACG and AGA* treatment guidelines recommend an ACTIVE test for *H. pylori*.¹,²

About 50% of patients with positive serology results do not have active *H. pylori* infections.¹

- At a 30% prevalence rate, serology has a positive predictive value of 63%.⁴,⁵
- At lower prevalence rates, clinical performance of the test declines further.³

Serology is an inadequate diagnostic method if *H. pylori* infection is suspected.¹

- Serologic tests cannot distinguish active *H. pylori* infection from past infection.³
- Guidelines recommend against the use of serological testing to detect *H. pylori*.¹
- Antibody tests should be avoided; positive results should be confirmed by an active test.¹

“[T]he modest incremental cost of active testing is well worth it for the additional accuracy achieved and for the avoidance of inappropriate treatment....”³

Breath or stool test – which is better for my patient?

Both the BreathTek® UBT and HpSA® offer high sensitivity and specificity, and meet the ACG and AGA guidelines.

**BreathTek®**

- Easy collection – exhale into bag #1, drink solution, wait 15 min., exhale into bag #2
- Fast 1 hour prior to test
- Suitable for ages 3–adult
- Not required, but recommended patient discontinue PPIs, antimicrobials, and bismuth 2 weeks prior to test.

**HpSA®**

- Stool collection at home
- No patient prep
- Suitable for all ages
- Discontinuing PPIs or bismuth not required

Many insurance plans have adopted and promote best practice guidance from ACG and AGA, and no longer recommend serology.

- Cigna, UnitedHealthcare, Anthem Blue Cross and Blue Shield, Empire Blue Cross and Blue Shield, Kaiser
The facts of *H. pylori*

- In the United States alone, one-third of the population is infected with *H. pylori*.
- There are 3.7 million cases of peptic ulcer disease (PUD) in the U.S. annually.
- One in 10 Americans are at risk of developing PUD.
- Most *H. pylori* bacteria are acquired during childhood and persist throughout life, if left untreated.
- *H. pylori* is a common chronic infection affecting 1 in 4 children in the U.S.
- 80%-90% of all ulcers are caused by or associated with *H. pylori*.⁶

References:

3. Enclose the card with the patient’s sample.

Steps for in-office sample collection and lab analysis:

Although the testing procedure will not change, the web-based Pediatric Urea Hydrolysis Rate Calculation Application (pUHR-CA) is required to determine pediatric patient test results. The pUHR-CA is available at: BreathTekKids.com

3. Add the test to your office as you would adult patients.*

1. Complete the pediatric UBT card with the following information—which is needed so that the lab can perform the analysis and UHR calculation:
   - Include collection date*
   - Patient ID: gender, age, height, and weight
   - Inclusive the card with the patient’s sample.

Warnings and Precautions

• Include the date of the diagnostic calculation. The Pranactin® Citric solution is taken orally as part of the diagnostic procedure and contains Phenylalanine (one of the protein components of Aspartame), 84 mg per dosage unit, and should be used with caution in diabetic patients.

• Ingestion of the Pranactin® Citric solution contains Phenylalanine, 12 ounces of typical diet cola soft drinks contains approximately 80 mg of Phenylalanine.

• A negative result does not rule out the possibility of a P. pylori infection. False-negative results do occur with the procedure. If clinic signs are suggestive of P. pylori infection, refer to a sample or an alternate method.

• False negative test results may be caused by:
  - Ingestion of proton pump inhibitors (PPIs) within 2 weeks prior to performing the BreathTek UBT. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to the BreathTek UBT, it may be a false-negative result and the test should be repeated 2 weeks after discontinuing the PPI treatment.
  - A positive result for a patient on a PPI could be considered positive and be acted upon.
  - Injection of antacid, or bismuth preparations within 2 weeks prior to performing the BreathTek UBT. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to performing the BreathTek UBT, it may be a false-negative result and the test should be repeated 2 weeks after discontinuing the PPI treatment.

• False positive test results may be caused by:
  - Ingestion of other gastric oropharyngeal pain (4.5% to include throat irritation, sore throat, throat burning), nausea (2.3%), restlessness (2.3%), stomach pain (1.0%), the following adverse events experienced by ≥1% of these patients were: vomiting (5.1%), abdominal pain (2.3%), or achlorhydria.

• During post-approval use of the BreathTek UBT in adults, the following adverse events have been identified: anaphylactic reaction, rash, burning sensation in the stomach, tingling in the skin, vomiting and diarrhea. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to establish a causal relationship to drug exposure.

• Adverse Events

During post approval use of the BreathTek UBT in adults, the following adverse events have been identified: allergic reaction, hypersensitivity, burning sensation in the oropharynx, pharyngitis, the following adverse events were observed among 99 subjects enrolled: 1 incidence each of cough, dry mouth and stomatitis. The following adverse events experienced by ≥1% of these patients were: vomiting (5.1%), abdominal pain (2.3%), or achlorhydria.

The BreathTek kids UBT is an approved as an aid in the initial diagnosis and post-treatment monitoring of H. pylori infection in adults and children aged 3 to 17 years.

H. pylori—don’t keep it in the family.

Pediatric guidelines recommend the UBT method to confirm H. pylori eradication:

• In 10–12 day eradication therapy is not reliable for use in the clinical setting3

References:


8. *In 10–12 day eradication therapy is not reliable for use in the clinical setting3

9. †European Society of Paediatric Gastroenterology, Hepatology and Nutrition.

10. ‡North American Society for Pediatric Gastroenterology, Hepatology and Nutrition.

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Learn more at BreathTekKids.com or call 888.637.3835.

A negative result does not rule out the possibility of a P. pylori infection. False-negative results do occur with the procedure.

3. False negative test results may be caused by:
   - Ingestion of proton pump inhibitors (PPIs) within 2 weeks prior to performing the BreathTek UBT. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to the BreathTek UBT, it may be a false-negative result and the test should be repeated 2 weeks after discontinuing the PPI treatment. A positive result for a patient on a PPI could be considered positive and be acted upon.
   - Ingestion of antacid, or bismuth preparations within 2 weeks prior to performing the BreathTek UBT. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to performing the BreathTek UBT, it may be a false-negative result and the test should be repeated 2 weeks after discontinuing the PPI treatment.

3. False positive test results may be caused by:
   - Ingestion of other gastric oropharyngeal pain (4.5% to include throat irritation, sore throat, throat burning), nausea (2.3%), restlessness (2.3%), stomach pain (1.0%), the following adverse events experienced by ≥1% of these patients were: vomiting (5.1%), abdominal pain (2.3%), or achlorhydria.

During post-approval use of the BreathTek UBT in adults, the following adverse events have been identified: anaphylactic reaction, rash, burning sensation in the stomach, tingling in the skin, vomiting and diarrhea. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to establish a causal relationship to drug exposure.

3. Adverse Events

During post approval use of the BreathTek UBT in adults, the following adverse events have been identified: allergic reaction, hypersensitivity, burning sensation in the oropharynx, pharyngitis, the following adverse events were observed among 99 subjects enrolled: 1 incidence each of cough, dry mouth and stomatitis. The following adverse events experienced by ≥1% of these patients were: vomiting (5.1%), abdominal pain (2.3%), or achlorhydria.

The BreathTek kids UBT is an approved as an aid in the initial diagnosis and post-treatment monitoring of H. pylori infection in adults and children aged 3 to 17 years.

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Diagnosing H. pylori in children

- In most children, H. pylori infection is not clinically apparent, even when causing chronic active gastritis.
- Children may present with gnawing or burning pain in the epigastrium, nausea, vomiting, or loss of appetite.
- Look for transmission between mother and child and siblings, which is most common. Another determinant is living in or originating from high-prevalence areas.

Confirming eradication is important because of:
- Poor compliance with medication.
- Reinfection as a result of intrafamilial transmission.
- Increasing antibiotic resistance.

- In children treated with standard H. pylori therapy, eradication rates have been decreasing over time, in part because of increased antibiotic resistance.

BreathTek UBT: Convenient, reliable, noninvasive

BreathTek UBT delivers excellent sensitivity (96%) and specificity (99%) for diagnosing H. pylori in pediatric patients.

<table>
<thead>
<tr>
<th>AGE</th>
<th>4-7 YEARS</th>
<th>8-12 YEARS</th>
<th>13-17 YEARS</th>
<th>COMBINED</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENSITIVITY</td>
<td>100%</td>
<td>100%</td>
<td>92%</td>
<td>96%</td>
</tr>
<tr>
<td>SPECIFICITY</td>
<td>100%</td>
<td>100%</td>
<td>98%</td>
<td>99%</td>
</tr>
</tbody>
</table>

Study design: A multicenter, open-label study. The primary endpoint analysis was conducted to determine the sensitivity and specificity of the BreathTek UBT UHR to the composite reference method criteria for the 176 evaluable cases. The table demonstrates the diagnostic performance of the BreathTek UBT (expressed as UHR) compared to the composite reference method criteria in pediatric patients ages 3 to 17 years.

False negative test results may be caused by:
- Ingestion of proton pump inhibitors (PPIs) within 2 weeks prior to performing the BreathTek UBT. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to the BreathTek UBT, it may be a false-negative result and the test should be repeated 2 weeks after discontinuing the PPI treatment. A positive result for a patient on a PPI could be considered positive and be acted upon.
- Ingestion of antimicrobials or bismuth preparations within 2 weeks prior to performing the BreathTek UBT.
- Premature POST-DOSE breath collection time for a patient with a marginally positive BreathTek UBT result.
- Post-treatment assessment with the BreathTek UBT less than 4 weeks after completion of treatment for the eradication of H. pylori.

False positive test results may be caused by urease associated with other gastric spiral organisms observed in humans, such as Helicobacter helminchi or ahlorhydria.

Please see accompanying BRIEF SUMMARY and enclosed Current Package Insert.
Brief Summary about BreathTek® UBT

Indications

The BreathTek® UBT for H. pylori Kit (BreathTek UBT Kit) is intended for use in the qualitative detection of urease associated with Helicobacter pylori infection in adult patients and pediatric patients 3 to 17 years old. The test may be used for monitoring treatment if used at least 4 weeks following completion of therapy. For these purposes, the system utilizes Infrared Spectrophotometry to measure the ratio of 13CO2 to 12CO2 in breath samples, in clinical laboratories or point-of-care settings. The Pediatric Urea Breath Test (UHR-CA), provided as a web-based calculation program, is required to obtain pediatric test results.

Important Safety Information:

Please read important safety information before using this product. Please see enclosed Current Package Insert.

Use this card when shipping breath samples from pediatric patients 3-17 years of age for analysis.

The pH UHR-CA is a web-based program to calculate the UHR-CA (https://BreathTekKids.com) to calculate the UHR.

H. pylori – don’t keep it in your family.

H. pylori is a common chronic infection affecting 1 in 4 children in the United States1

- Transmitted predominantly among family members2

- Highest rates of infection occur in children younger than 10 years of age2

- May become chronic without treatment3

- May cause duodenal ulcers, gastric ulcers, and progressive gastric mucosal damage in children4

Pediatric guidelines recommend the UBT method to confirm H. pylori eradication5

- The urea breath test (UBT) method, generally considered the gold standard in adults for diagnosis of H. pylori, is recommended for use with children by NASPGHAN†8,9

- 9 in 10 declared serology is not reliable for use in the clinical setting8

- H. pylori infection in adults and children ages 3 to 17 years

Warning:

- The pH UHR-CA is intended for use with children by NASPGHAN†8,9

- Use with caution in patients with difficulty swallowing or who may be at high risk of aspiration due to medical or physical conditions.

- There is no information on use of the Pranactin-Citric solution during pregnancy. Please see accompanying BRIEF SUMMARY and enclosed Current Package Insert.

- The pH UHR-CA calculation is not intended for use in determining the presence of Helicobacter pylori infection in pediatric patients. DOB results cannot be used to calculate the UBT metrics to determine if H. pylori infection in pediatric patients. DOB results cannot be used to determine the infection status of pediatric patients. Use the web-based pH UHR-CA (https://BreathTekKids.com) to calculate the UHR.

- Safety and effectiveness has not been established in children below the age of 3 years.

Adverse Events

During post-approval use of the BreathTek® UBT in adults, the following adverse events have been identified: stomach ache/belly pain (1.1%), nausea (2.3%), oropharyngeal pain (4.5% to include throat irritation, sore throat, throat burning), headache (1.1%), and diarrhea (1.1%). Most of the adverse events were experienced by patients within minutes to hours of oropharyngeal pain and diarrhea, and during post treatment monitoring of H. pylori.

In two clinical studies conducted in 176 (analyzed) pediatric patients ages 3 to 17 years to determine the initial diagnosis and treatment of H. pylori, 108 subjects were reported to have experienced at least one adverse event. The following adverse events were observed among ≥1% of these patients: vomiting (5.1%), headache (2.3%), post-treatment monitoring (2.3%), and diarrhea (1.1%). Most of the adverse events were experienced by patients within minutes to hours of treatment of the Pranactin-Citric solution.

In another clinical study comparing the pH UHR-CA and POCOn® in pediatric patients ages 3 to 17 years to determine the infection in adults and children ages 3 to 17 years old, the test may be used for monitoring treatment if used at least 4 weeks following completion of therapy. For these purposes, the system utilizes Infrared Spectrophotometry to measure the ratio of CO2 to 12CO2 in breath samples, in clinical laboratories or point-of-care settings. The Pediatric Urea Breath Test (UHR-CA), provided as a web-based calculation program, is required to obtain pediatric test results.

The BreathTek® UBT Kit is for administration by a health-care professional, as ordered by a licensed health-care practitioner.

Three available testing options for your convenience

Use this card when shipping breath samples from pediatric patients 3-17 years of age for analysis.

The pH UHR-CA is a web-based program to calculate the UHR-CA (https://BreathTekKids.com) to calculate the UHR.

<table>
<thead>
<tr>
<th>IN OFFICE</th>
<th>IN LAB</th>
<th>IN OFFICE AND LAB</th>
</tr>
</thead>
</table>

For more information, visit BreathTek.com or call 888.637.3835 for an appointment with a BreathTek® UBT representative.

References:

6. Pranactin-Citric solution contains these ingredients. Use with caution in patients with difficulty swallowing or who may be at high risk of aspiration due to medical or physical conditions.
7. The pH UHR-CA calculation is not intended for use in determining the presence of Helicobacter pylori infection in pediatric patients. DOB results cannot be used to calculate the UBT metrics to determine if H. pylori infection in pediatric patients. DOB results cannot be used to determine the infection status of pediatric patients. Use the web-based pH UHR-CA (https://BreathTekKids.com) to calculate the UHR.
Brief Summary about BreathTek UBT

**Helicobacter pylori**

The BreathTek® UBT Kit (BreathTek UBT Kit) is intended for use in the qualitative detection of urease associated with *H. pylori* in breath samples obtained from children ages 3 to 17 years old.

**Eradication**

The BreathTek® UBT Kit (BreathTek UBT Kit) may be used for monitoring treatment if used at least 4 weeks following completion of therapy. For these purposes, the system utilizes an Infrared Spectrophotometer for the measurement of the ratio of 13CO2 to 12CO2 in breath samples, in clinical laboratories or point-of-care settings. The Pediatric Urea Hydrolysis Rate (UHR) calculation, provided as a web-based calculation program, is required to obtain pediatric test results.

**Warnings and Precautions**

• The BreathTek UBT Kit is for administration by a health care professional, as ordered by a licensed health care practitioner.

• The BreathTek® UBT for *H. pylori* is approved as an aid in the initial diagnosis and post-treatment monitoring of *H. pylori* infection in adults and children ages 3 to 17 years. The test may be used for monitoring treatment if used at least 4 weeks following completion of therapy. For these purposes, the system utilizes an Infrared Spectrophotometer for the measurement of the ratio of 13CO2 to 12CO2 in breath samples, in clinical laboratories or point-of-care settings. The Pediatric Urea Hydrolysis Rate (UHR) calculation, provided as a web-based calculation program, is required to obtain pediatric test results.

**Pediatric Use**

• The BreathTek UBT Kit (BreathTek UBT Kit) is intended for use in the qualitative detection of urease associated with *H. pylori* in breath samples obtained from children ages 3 to 17 years old.

• The BreathTek UBT Kit (BreathTek UBT Kit) may be used for monitoring treatment if used at least 4 weeks following completion of therapy. For these purposes, the system utilizes an Infrared Spectrophotometer for the measurement of the ratio of 13CO2 to 12CO2 in breath samples, in clinical laboratories or point-of-care settings. The Pediatric Urea Hydrolysis Rate (UHR) calculation, provided as a web-based calculation program, is required to obtain pediatric test results. The BreathTek® UBT for *H. pylori* is approved as an aid in the initial diagnosis and post-treatment monitoring of *H. pylori* infection in adults and children ages 3 to 17 years.

**Information on Use of the Pranactin-Citric Solution**

• The BreathTek® UBT Kit (BreathTek UBT Kit) is intended for use in the qualitative detection of urease associated with *H. pylori* in breath samples obtained from children ages 3 to 17 years old.

• The BreathTek® UBT Kit (BreathTek UBT Kit) may be used for monitoring treatment if used at least 4 weeks following completion of therapy. For these purposes, the system utilizes an Infrared Spectrophotometer for the measurement of the ratio of 13CO2 to 12CO2 in breath samples, in clinical laboratories or point-of-care settings. The Pediatric Urea Hydrolysis Rate (UHR) calculation, provided as a web-based calculation program, is required to obtain pediatric test results. The BreathTek® UBT for *H. pylori* is approved as an aid in the initial diagnosis and post-treatment monitoring of *H. pylori* infection in adults and children ages 3 to 17 years.
Could PPI therapy be an underlying condition?

About 60% of adult patients are already taking a PPI when they initially seek a physician’s help for their GI symptoms. The root cause may be *H. pylori*. 
The BreathTek® UBT Kit (BreathTek UBT Kit) is intended for use in the qualitative detection of urease activity with H. pylori in the human stomach and is indicated as an aid in the initial diagnosis and post-treatment monitoring of H. pylori infection in adult patients and pediatric patients 3 to 17 years old. The test may be used for monitoring treatment if used at least 4 weeks following completion of therapy. For these purposes, the system utilizes an Infrared Spectrophotometer for the measurement of the ratio of $^{13}$CO$_2$ to $^{12}$CO$_2$ in breath samples, in clinical laboratories or point-of-care settings. The Pediatric Urea Hydrolysis Rate Calculation Application (pUHR-CA), provided as a web-based calculation program, is required to obtain pediatric test results.

**Warnings and Precautions**

- For in vitro diagnostic use only. The Pranactin®-Citric solution is taken orally as part of the diagnostic procedure and contains Phenylalanine (one of the protein components of Aspartame), 84 mg per dosage unit. (For reference, 12 ounces of typical diet cola soft drinks contain approximately 80 mg of Phenylalanine.)
- A negative result does not rule out the possibility of H. pylori infection. False negative results do occur with this procedure. If clinical signs are suggestive of H. pylori infection, retest with a new sample or an alternate method.
- False negative test results may be caused by:
  - Ingestion of proton pump inhibitors (PPIs) within 2 weeks prior to performing the BreathTek UBT. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to the BreathTek UBT, it may be a false-negative result and the test should be repeated 2 weeks after discontinuing the PPI treatment. A positive result for a patient on a PPI could be considered positive and be acted upon.
  - Ingestion of antibiotics, or bismuth preparations within 2 weeks prior to performing the BreathTek UBT.
  - Premature POST-DOSE breath collection time for a patient with a marginally positive BreathTek UBT result.
  - Post-treatment assessment with the BreathTek UBT less than 4 weeks after completion of treatment for the eradication of H. pylori.
- False positive test results may be caused by:
  - Urease associated with other gastric spiral organisms observed in humans such as Helicobacter heilmanni or achlorhydria.
  - Oral contamination associated with urease containing bacteria especially when not using the straw provided in the BreathTek UBT Kit.

**Adverse Events**

During post-approval use of the BreathTek UBT in adults, the following adverse events have been identified: anaphylactic reaction, hypersensitivity, rash, burning sensation in the stomach, tingling in the skin, vomiting and diarrhea. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to establish a causal relationship to drug exposure.

In two clinical studies conducted in 176 (analyzed) pediatric patients ages 3 to 17 years to determine the initial diagnosis and post treatment monitoring of H. pylori, the following adverse events experienced by ≥1% of these patients were: vomiting (5.1%), oropharyngeal pain (4.5% to include throat irritation, sore throat, throat burning), cough (4.3%), abdominal discomfort (4.3%), and dry mouth (4.2%). The following adverse events were observed among the 99 subjects enrolled: 2 incidences of headache, and 1 incidence of each of cough, dry mouth and acute upper respiratory infection.

**Pharmaceutical, Inc; 2016. References: 1.**
Patients taking PPIs may be tested with BreathTek® UBT for *H. pylori*

- It is still recommended that antibiotics, PPIs, or bismuth preparations not be taken within 2 weeks prior to administering the BreathTek UBT®.
- If the patient is taking a PPI and tests positive for *H. pylori* infection, the result is considered positive and eradication therapy can be started immediately. If the test is negative, it may be a false negative and results should be confirmed with a second breath test 2 weeks after discontinuing the PPI.
- The effect of histamine 2-receptor antagonists (H2RAs) may reduce urease activity on urea breath tests. H2RAs may be discontinued for 24 to 48 hours before the BreathTek UBT®.
- The use of antacids does not appear to affect the accuracy of the BreathTek UBT®.

Pooled data from 9 published studies of *H. pylori*-positive patients (N=626) confirm the performance of the UBT method in patients taking PPIs.

Please see accompanying BRIEF SUMMARY and enclosed Current Package Insert.

Learn more at BreathTek.com or call 888.637.3835.

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**Adverse Events**

- Patients who are hypersensitive to mannitol, citric acid or Aspartame should avoid taking the drug solution as this can cause anaphylactic reaction, hypersensitivity, rash, burning sensation in the stomach, tingling in the skin, vomiting and diarrhea. Because each of cough, dry mouth and acute upper respiratory infection.

- During post-approval use of the BreathTek UBT in adults, the following adverse events have been identified: anaphylactic reaction, hypersensitivity, rash, burning sensation in the stomach, tingling in the skin, vomiting and diarrhea. Because each of cough, dry mouth and acute upper respiratory infection.

- In another clinical study comparing the UBiT®-IR300 and POCone® in pediatric patients ages 3 to 17 years, the following adverse events were observed among the 99 subjects enrolled: 2 incidences of headache, and 1 incidence of nausea, dizziness, constipation, vomiting, and diarrhea. Most of the adverse events were experienced by patients within minutes to hours of ingestion of the Pranactin-Citric solution.

- In two clinical studies conducted in 176 (analyzed) pediatric patients ages 3 to 17 years to determine the initial diagnosis and post treatment monitoring of *H. pylori* infection, the result is considered positive and eradication therapy can be started immediately. If the test is negative, it may be a false negative and results should be confirmed with a second breath test 2 weeks after discontinuing the PPI. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to the BreathTek UBT, it may be a false-negative and results should be confirmed with a second breath test 2 weeks after discontinuing the PPI.

- Patients taking PPIs may be tested with BreathTek® UBT for *H. pylori*. The BreathTek® UBT for *H. pylori* is intended for use in the qualitative detection of urease activity in the presence of *H. pylori* infection. It is a noninvasive procedure. If clinical signs are suggestive of *H. pylori* infection, retest with a new sample or an alternate method.

- The BreathTek® UBT for *H. pylori* is intended for use in the qualitative detection of urease activity in the presence of *H. pylori* infection. It is a noninvasive procedure. If clinical signs are suggestive of *H. pylori* infection, retest with a new sample or an alternate method.

- False negative test results may be caused by:
  - Ingestion of antibiotics, or bismuth preparations within 2 weeks prior to performing the BreathTek UBT. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to the BreathTek UBT, it may be a false-negative and results should be confirmed with a second breath test 2 weeks after discontinuing the PPI.
  - False negative results do occur with this test method.
  - Ingestion of proton pump inhibitors (PPIs) within 2 weeks prior to performing the BreathTek UBT. If a negative result is obtained from a patient ingesting a PPI within 2 weeks prior to the BreathTek UBT, it may be a false-negative and results should be confirmed with a second breath test 2 weeks after discontinuing the PPI.

- The safety of using the BreathTek UBT Kit during pregnancy and lactation is not established.

- The effect of histamine 2-receptor antagonists (H2RAs) may reduce urease activity on urea breath tests. H2RAs may be discontinued for 24 to 48 hours before the BreathTek UBT®.

- Ingestion of histamine 2-receptor antagonists (H2RAs) and the use of antacids do not appear to affect the accuracy of the BreathTek UBT®.