LABTESTCONNECT

H. pylori BreathTek® UBT

PAML
PATHOLOGY ASSOCIATES MEDICAL LABORATORIES

ORDER CODES:
HPBTAD (Adult)
HPBRT (Peds)

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.

Quick Facts

- 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
2. American Gastroenterological Association Technical Review on the Evaluation of Dyspepsia. Gastroenterology 2005;129:1756-1780
3. Helicobacter pylori Diagnosis and Management. Gastroenterol Clin N Am 35 (2006) 229-247

H. pylori BreathTek® UBT

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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 Axid.
- 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

H. PYLORI BREATH TEST	
DESCRIPTION	Helicobacter pylori Breath Test
METHOD	Infared spectrophotometry
ORDER CODES	**HPBRT** (Peds) **HPBTAD** (Adults)
CPT CODES	83013, 83014 (sample collection)
SPECIMEN REQUIREMENTS	**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 Axid. **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.

Otsuka
Medical Device Division of
Otsuka America Pharmaceutical, Inc.

Urea Breath Test for *H. pylori*
BreathTek®

Rx only

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 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 and point-of-care settings. The Pediatric Urea Hydrolysis Rate Calculation Application (*p*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.

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.[2, 3] *H. pylori* is associated with a number of GI conditions including chronic gastritis, peptic ulcer disease, and gastric malignancy.[4, 5] 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. Biopsy 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.[6]

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 ^{13}C-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 3 gram dose of Pranactin-Citric is supplied in a polyethylene-lined foil pouch and contains 75 mg of ^{13}C-urea, citric acid[7], aspartame and mannitol. ^{13}C-urea is the diamide of ^{13}C-carbonic acid and is highly soluble in water (1 gram per mL at 25°C). It has the following chemical formula: $^{13}CH_4N_2O$. 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 composed of 98.9% ^{12}C-urea and 1.1% ^{13}C-urea.

3.2 *Principle of the Test*

Pranactin-Citric drug product is a component of the BreathTek UBT Kit. Three (3) g of reconstituted Pranactin-Citric containing 75 mg of ^{13}C-urea is ingested by the patient. In the presence of urease associated with gastric *H. pylori*, ^{13}C-urea [$(NH_2)_2\,{}^{13}CO$] is decomposed to $^{13}CO_2$ and NH_4^+ according to the following equation:

$$(NH_2)_2\,{}^{13}CO + H_2O + 2H^+ \xrightarrow{\textit{H. pylori}\ \text{urease}} {}^{13}CO_2 + 2NH_4^+$$

The $^{13}CO_2$ is absorbed in the blood, and then exhaled in the breath. It results in an increase in the ratio of $^{13}CO_2$ to $^{12}CO_2$ 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 or POCone® Infrared Spectrophotometer located at your clinical laboratory and point-of-care settings.

In the absence of gastric *H. pylori*, the ^{13}C-urea does not produce $^{13}CO_2$ in the stomach. The ratio of $^{13}CO_2$ in the POST-DOSE breath sample remains essentially the same as the BASELINE.

3.3 *Adjustment of Endogenous CO_2 Production with UHR Calculation in Pediatric Patients*

The measured difference between the ratios of $^{13}CO_2/^{12}CO_2$ 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 adults. It is known that the measured Delta over Baseline (DOB) is a function of anthropometric variables, which determine the rate of CO_2 production.[8]

While the effect of the CO_2 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:

$$\text{UHR } (\mu g/min) = \text{DOB} \times CO_2 \text{ Production Rate} \times 0.3427$$

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, retest with 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:
- Urease associated with other gastric spiral organisms observed in humans such as *Helicobacter heilmannii*.
- Achlorhydria[9]
- Oral contamination associated with urease 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. Swollen 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 pediatric test results, the UHR results must be calculated. DOB results in conjunction with Pediatric Urea Hydrolysis Rate Calculation Application (*p*UHR-CA), provided as a web-based calculation program, is required to obtain pediatric test results. DOB results **cannot** be used to determine the infection status of pediatric patients.

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 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 (1.1%), and diarrhea (1.1%). Most of the adverse events were experienced by the 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 observed among the 99 subjects enrolled: 2 incidences of headache, 1 incidence each of cough, dry mouth and acute upper respiratory infection.

6 Shelf Life and Storage

The BreathTek UBT Kit should be stored at 15°-30°C (59°-86°F). Pranactin-Citric has an expiration date of 48 months at 15°-30°C (59°-86°F). Do not use beyond the expiration date stated on the label.

7 Patient Preparation

7.1 Remind the patient that Pranactin-Citric contains phenylalanine (one of the protein components of Aspartame). Phenylketonurics restrict dietary phenylalanine.

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 administering 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 PPI could be considered positive and be acted upon.

7.4 The effect of histamine 2-receptor antagonists (H_2RAs) may reduce urease activity on urea breath tests.[12] H_2RAs 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) "How To" guide with One (1) patient p-UHR card
- 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

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

8.1.2 Materials needed but not provided

- A timer capable of timing an interval up to 15 minutes

8.1.3 Instruments and Software

- In adult patients, an Infrared Spectrophotometer (UBiT-IR300 or POCone, *Otsuka Pharmaceutical Co., Ltd.)* is required for analysis of breath samples.
- In pediatric patients,
  – Use the UBiT-IR300 or POCone Infrared Spectrophotometer to analyze the breath samples.
  – Use of the Pediatric Urea Hydrolysis Rate Calculation Application (*p*UHR-CA), as a web-based calculation program, is required to obtain the test result.
  – Go to: https://BreathTekKids.com to use the web-based *p*UHR-CA to calculate the UHR and obtain pediatric test results.

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 plastic sample transport bag for transport of the breath samples.

8.2.10 When shipping breath sample bags from pediatric patients to a laboratory for analysis, complete the pediatric UHR card by entering collection date, patient ID, gender, age, height and weight. Place the completed card inside the sample transport bag along with the collected breath samples and the laboratory's test requisition form.

9 Quality Control

Complete operating information, including self-diagnostic instrument routines and user maintenance procedures provided in the Instruction Manuals for the UBiT -IR300 Spectrophotometer, the UBiT-AS10 Autosampler, the POCone Infrared Spectrophotometer and the POC-AS10 Auto sampler, 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 $^{13}CO_2$ to $^{12}CO_2$ in breath samples is determined by Infrared Spectrophotometer, either UBiT-IR300 or POCone.

10.1.2 Calculation of Results

The result is provided as the Delta over Baseline (DOB) which is the difference between the ratio of $^{13}CO_2$ / $^{12}CO_2$ 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 Cutoff 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 ^{13}C-urea. Analysis of the breath samples was performed by gas isotope ratio mass spectrometry (GIRMS). 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).

Figure 1a. Data Distribution before the Cutoff for Meretek UBT

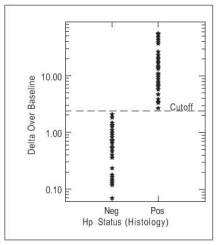
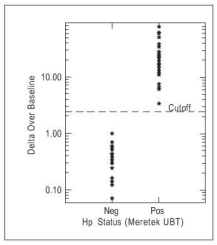


Figure 1b. Data Distribution before the Cutoff for BreathTek® UBT



10.1.4 Interpretation of Results for Adults

A DOB value of ≥ 2.4 is interpreted as diagnostically positive indicating the presence of urease associated with *H. pylori*. A DOB value of < 2.4 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 provides the interpretation of the DOB result on the test strip.

10.2 Pediatrics

10.2.1 The Test Method

The ratio of $^{13}CO_2$ to $^{12}CO_2$ in breath samples from children aged 3 - 17 years is determined by the UBiT-IR300 or POCone Infrared Spectrophotometer. Although the DOB result of the BreathTek UBT is provided by the UBiT-IR300 or POCone Infrared Spectrophotometer, urea hydrolysis rate (UHR) using the *p*UHR-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 *p*UHR-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 CO_2 production rate in that patient. The UHR is calculated as shown below:

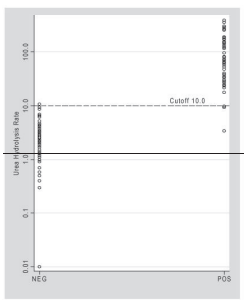
$$\text{UHR } (\mu g/min) = \text{DOB} \times CO_2 \text{ Production Rate} \times 0.3427$$

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.[8] 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 UBiT-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.[10,11] 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 ≥ 10 µg/min is interpreted as diagnostically positive indicating the presence of urease associated with *H. pylori*. A UHR value of < 10 µg/min is interpreted as diagnostically negative indicating the absence of urease associated with *H. pylori*. The same UHR cutoff value applies to both initial diagnosis and post-treatment monitoring of *H. pylori* infection in children. The web-based *p*UHR-CA program provides the interpretation of the UHR result on the output of the calculation.

Go to: https://BreathTekKids.com to use the web-based *p*UHR-CA program.

11 Limitations of the Test

11.1 The BreathTek UBT should not be used until 4 weeks or more after the end of treatment for the 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 *p*UHR-CA to calculate the UHR to obtain pediatric test results. Go to: https://BreathTekKids.com.

11.6 The web-based *p*UHR-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 outcome 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 UBiT-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 two (2) independent double-blind clinical field trials which involved treatment of *H. pylori* infection. The studies included 499 adult patients with duodenal ulcer disease at 75 clinical sites in the United States. Patients were tested for *H. pylori* infection initially by the composite reference method; histopathology, microbiological culture, urease detection test compared to the Meretek UBT, and at various post-treatment intervals throughout the study (using histopathology, microbiological culture, and the Meretek UBT). In these clinical trials, patients were treated with various combinations of clarithromycin, omeprazole and placebo. Note, however, that there is no evidence that differing treatment regimens affect the performance of the Meretek UBT.

1. **Histopathology**
   Biopsy specimens, fixed with 10% buffered formalin were cut into 4-mm sections, stained with Genta stain and examined by an experienced pathologist.
2. **Microbiologic culture**
   Culture was performed using fresh blood-based media, both selective and non-selective, at 37°C in 12% CO_2 in air with 98% humidity. *H. pylori* were identified by Gram stain, typical colony morphology, and biochemical properties (production of oxidase, catalase and urease).
3. **Urease detection test**
   A biopsy specimen was tested for urease activity with the urease detection test according to the instructions in its package insert.
4. **The Meretek UBT for *H. pylori***
   The diagnostic Meretek UBT was performed in accordance with procedures described in its package insert.

b. Results

Clinical performance results are presented in two-way contingency tables. In Table 1, the Meretek UBT results are compared with the composite reference method results (urease detection test, histology, and culture) for the initial patient visit[10]. In the same study, the Meretek UBT results were also compared with urease detection test and histology. The relative sensitivity and specificity of Meretek UBT for initial visit are 92.8% (95% CI: 90, 95) and 94.1% (95% CI: 71, 100), respectively, compared to urease detection test, and are 95.2% (95% CI: 93, 97) and 90.0% (95% CI: 74, 98), respectively, compared to histology. In Table 2, the Meretek UBT results are compared with the composite reference method results (histology and culture) for the post-treatment visits which occurred 4 weeks or more after end of treatment.

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 1. Comparison with Composite Reference Method* in Adult Patients for Initial Visit (pre-treatment)

	Meretek UBT Results		
Endoscopy	Positive	Negative	Total
Positive	395	20	415
Negative	3	26	29
Total	398	46	444

* Composite reference method [10,11] includes the urease detection test, histology, and culture for pre-treatment diagnosis

Sensitivity: 95.2% [95% CI: (93, 97)]
Specificity: 89.7% [95% CI: (73, 98)]

BreathTek® UBT for *H. pylori* Kit

Table 2. Comparison with Composite Reference Method* in Adult Patients for Post-Treatment Visits (4 weeks or more after End of Treatment (EOT)

	Meretek UBT Breath Test Results							
	1 Month EOT		3 Months EOT		6 Months EOT		1-6 Months Combined	
Endoscopy	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg
Positive	187	6	123	8	91	5	401	19
Negative	5	97	4	87	2	80	11	264
Sensitivity (95% CI)	96.9 (93, 99)		93.9 (88, 97)		94.8 (88, 98)		95.5 (93, 97)	
Specificity (95% CI)	95.1 (89, 98)		95.6 (89, 99)		97.6 (92, 100)		96.0 (93, 98)	

* Composite reference method [10,11] includes histology, urease detection test and culture for post-treatment monitoring.

Please note that the post-treatment performance characteristics at 1, 3 and 6 months after therapy are not statistically different. Therefore, the single best estimates of sensitivity and specificity are presented in the 1-6 Months Combined column.

Negative Predictive Value (NPV) for Post-Treatment Monitoring

Given the post-treatment sensitivity (95.5%) and specificity (96.0%) observed in these studies, and assuming a treatment efficacy of 90% (10% prevalence of residual *H. pylori* infection), the NPV of the Meretek UBT is greater than 99%. When efficacy of treatment drops to 50%, the NPV is still greater than 95%.

13.4.2 Comparison of the BreathTek UBT with the Meretek UBT 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 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 (≥1-hour fast) with Meretek UBT

	BreathTek UBT Results		
Meretek UBT	Positive	Negative	Total
Positive	105	1	106
Negative	1	145	146
Total	106	146	252

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)]

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

A multi-center prospective clinical trial was conducted to compare the UBiT-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 UBiT-IR300 Infrared Spectrophotometer (refer to the Application Note, ^{13}C-Urea Breath Test using the UBiT-IR300 Infrared Spectrophotometry System).

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

Table 4. Agreement of UBiT-IR300 and GIRMS for ^{13}C urea breath test

	GIRMS Results		
UBiT-IR 300 Results	Positive	Negative	Total
Positive	115	1	116
Negative	2	202	204
Total	117	203	320

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: 99.51% [95% CI: (97.49, 99.97)]

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

A multi-center, prospective study was conducted to compare the POCone Infrared Spectrophotometer to the UBiT-IR300 Infrared Spectrophotometer for measuring $^{13}CO_2$ 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 POCone Infrared Spectrophotometer (refer to the Application Note, ^{13}C-Urea Breath Test using the POCone Infrared Spectrophotometry System).

Table 5 shows the percent agreement of the POC-one results with the UBiT-IR300 results. Overall agreement was 99.55 percent.

Table 5. Agreement of POCone and UBiT-IR300 for the ^{13}C urea breath test

	UBiT-IR300 Results		
POCone Results	Positive	Negative	Total
Positive	86	1	87
Negative	0	133	133
Total	86	134	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

13.5.1 Clinical Performance in Clinical Trials for Initial Diagnosis in 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 evaluable 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

	^{13}C-UBT UHR							
	Age 3-5 Years		Age 6-12 Years		Age 13-18 Years		All Age Groups Combined	
Endoscopic Composite Reference Method	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg
Infected	3	0	21	0	22	2	46	2
Not Infected	0	17	0	62	1	48	1	127
Sensitivity (95% CI)	100.0 (29.2, 100.0)		100.0 (83.9, 100.0)		91.7 (73.0, 99.0)		95.8 (85.7, 99.3)	
Specificity (95% CI)	100.0 (80.4, 100.0)		100.0 (94.2, 100.0)		98.0 (89.0, 100.0)		99.2 (95.7, 100.0)	

13.5.2 Clinical Performance in Clinical Trials for Post Treatment Monitoring in Pediatric Patients

a. Experimental Design

The study was a multi-center, open-labeled study designed to compare the BreathTek UBT with endoscopic methods for the post treatment monitoring of *H. pylori* in the pediatric population. Pediatric patients 3 to 17 years old who enrolled in this study had participated in the initial diagnosis study described above, and were diagnosed by upper endoscopy to be infected with *H. pylori* using the composite reference method criteria (e.g., histology, culture and urease test).

The study enrolled 22 pediatric patients at three (3) U.S. investigational sites (Houston, Texas, Detroit, Michigan and Huntington, West Virginia) of which 20 subjects were evaluable for analysis. The reasons for data exclusion were due to invalid UBT results and EDG was not performed.

The primary outcome variable of the BreathTek UBT was the UHR in comparison to the endoscopic findings of the composite reference method criteria. To determine the infection status following eradication therapy, these criteria were interpreted to include test results for all three *H. pylori* testing methods (histology, culture, rapid urease test). Results for all three *H. pylori* testing methods were available for all of the 20 evaluable cases. The primary endpoint analysis was conducted to determine the sensitivity and specificity of the BreathTek UBT (UHR) to the endoscopic composite reference method criteria for the 20 evaluable cases.

b. Results – Comparison of BreathTek UBT (UHR) to the Composite Reference Method Criteria

The observed sensitivity for UHR when compared to the composite reference method criteria is 83.3%, and the observed specificity is 100% (Table 7). Because of the small sample size, the results, including the 95% confidence intervals around the sensitivity and specificity, should be interpreted with caution.

Table 7. Comparison of Composite Reference Method Criteria and BreathTek UBT UHR in Pediatric Patients for Post Treatment Monitoring

		^{13}C-UBT UHR	
		N=20	
		Pos	Neg
Composite Reference Method Criteria	Infected	5	1
	Eradicated	0	14
Sensitivity		83.3% [95% CI: (40.2, 99.2)]	
Specificity		100% [95% CI: (77.0, 100.0)]	

BreathTek® UBT for *H. pylori* Kit

13.5.3 Comparison of UBiT-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 UBiT-IR300 in measuring $^{13}CO_2/^{12}CO_2$ ratio in breath samples when used together with the BreathTek UBT Kit and the *p*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 *H. pylori* eradication therapy.

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

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

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

	POCone UHR		
UBiT-IR300 UHR	Positive	Negative	Total
Positive	24	0	24
Negative	0	71	71
Total	24	71	95

Percent Overall Agreement: 100% [95% CI: (96.2, 100.0)]
Percent Positive Agreement: 100% [95% CI: (85.5, 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

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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 1.888.637.3835 or visit www.BreathTek.com.

16 Trademarks

BreathTek® is a registered trademark of Otsuka America Pharmaceutical, Inc.
Pranactin®-Citric, UBiT®-IR300 and POCone® are registered trademarks of Otsuka Pharmaceutical Co., Ltd.

17 Labeling Revision Information

Revision: January 2016

05US16IBR0003

ICD-10 Coding Guide

CPT coding information

NEW ICD-10 Codes

Two unique CPT codes are applicable to administration and analysis of BreathTek® UBT for *H. pylori*. The test is covered by Medicare and most insurance providers.

Procedural codes for *H. pylori* testing

83014	Drug administration and sample collection
83013	*Helicobacter pylori* breath test analysis for urease activity, non-radioactive isotope

Diagnosis codes*†

Several codes associated with *H. pylori* testing include:

Stomach

C16.9 Malignant neoplasm of stomach, unspecified; Gastric cancer NOS

C88.4 Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]

K25.0 Acute gastric ulcer with hemorrhage

K25.0 Acute gastric ulcer with hemorrhage ***AND***
K56.60 Unspecified intestinal obstruction

K25.4 Chronic or unspecified gastric ulcer with hemorrhage

K25.4 Chronic or unspecified gastric ulcer with hemorrhage ***AND***
K56.60 Unspecified intestinal obstruction

K25.7 Chronic gastric ulcer without hemorrhage or perforation

K25.7 Chronic gastric ulcer without hemorrhage or perforation ***AND***
K56.60 Unspecified intestinal obstruction

K25.9 Gastric ulcer, unspecified as acute or chronic, without hemorrhage or perforation

K25.9 Gastric ulcer, unspecified as acute or chronic, without hemorrhage or perforation ***AND***
K56.60 Unspecified intestinal obstruction

K30 Functional Dyspepsia

Gastritis

K29.00 Acute gastritis without bleeding

K29.01 Acute gastritis with bleeding

K29.30 Chronic superficial gastritis without bleeding

K29.31 Chronic superficial gastritis with bleeding

K29.40 Chronic atrophic gastritis without bleeding

K29.41 Chronic atrophic gastritis with bleeding

K29.50 Unspecified chronic gastritis without bleeding

K29.51 Unspecified chronic gastritis with bleeding

K29.70 Gastritis, unspecified, without bleeding

K29.71 Gastritis, unspecified, with bleeding

K29.80 Duodenitis without bleeding

K29.81 Duodenitis with bleeding

K29.90 Gastroduodenitis, unspecified, without bleeding

K29.91 Gastroduodenitis, unspecified, with bleeding

Duodenum

K26.0 Acute duodenal ulcer with hemorrhage

K26.0 Acute duodenal ulcer with hemorrhage ***AND***
K56.60 Unspecified intestinal obstruction

K26.3 Acute duodenal ulcer without hemorrhage or perforation

K26.3 Acute duodenal ulcer without hemorrhage or perforation ***AND***
K56.60 Unspecified intestinal obstruction

K26.4 Chronic or unspecified duodenal ulcer with hemorrhage

K26.4 Chronic or unspecified duodenal ulcer with hemorrhage ***AND***
K56.60 Unspecified intestinal obstruction

K26.9 Duodenal ulcer, unspecified as acute or chronic, without hemorrhage or perforation

K26.9 Duodenal ulcer, unspecified as acute or chronic, without hemorrhage or perforation ***AND***
K56.60 Unspecified intestinal obstruction

Other

B96.81 *Helicobacter pylori* as the cause of diseases classified elsewhere

This reimbursement information is being provided to help the health care professional understand and comply with billing and reimbursement requirements that may apply to products. Use of codes identified here does not guarantee coverage or payment at any specific level. Consult the patient's insurance carrier to verify coverage and reimbursement information.

**Partial list: Please contact individual plans for a list of codes that support medical necessity.*
†The listing of diagnosis codes does not imply that the use of a urea breath test is suitable for all of the conditions shown.

What is BreathTek UBT?

The BreathTek UBT Kit is intended for use in the qualitative detection of urease associated with *H. pylori* in the human stomach and 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 BreathTek UBT Kit is for administration by a health care professional, as ordered by a licensed health care practitioner.

Test. Treat. Confirm.

- **Test:** Diagnose if *H. pylori* is the underlying issue[1]
- **Treat:** Consider an FDA-recommended therapy for patients who test positive[2,3]
- **Confirm:** Test again 4 weeks after the end of treatment to allow time for adequate recolonization if eradication is unsuccessful[4,5]

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

Please see accompanying BRIEF SUMMARY and enclosed Current Package Insert.

Otsuka
Medical Device Division of
Otsuka America Pharmaceutical, Inc.

BreathTek®

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 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 (*p*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.

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, and should be used with caution in diabetic patients. (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 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 heilmannii* or achlorhydria.
- If particulate matter is visible in the reconstituted Pranactin-Citric solution after thorough mixing, the solution should not be used.
- Patients who are hypersensitive to mannitol, citric acid or Aspartame should avoid taking the drug solution as this drug 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.
- No information is available on use of the Pranactin-Citric solution during pregnancy.
- For pediatric test results, the Urea Hydrolysis Rate (UHR) results must be calculated. The Delta over Baseline (DOB) results are only used to calculate the UHR metrics to determine *H. pylori* infection in pediatric patients. DOB results **cannot** be used to determine the infection status of pediatric patients. Use the web-based *p*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: 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), nausea (2.3%), restlessness (2.3%), stomach ache/belly pain (1.1%), 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 observed among the 99 subjects enrolled: 2 incidences of headache, and 1 incidence each of cough, dry mouth and acute upper respiratory infection.

May 2014 05US14EBP1200

Please see accompanying Current Package Insert.

References: 1. Talley NJ, Vakil N; Practice Parameters Committee of the American College of Gastroenterology. Guidelines for the management of dyspepsia. *Am J Gastroenterol.* 2005;100(10):2324-2337. **2.** Chey WD, Wong BCY; Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. *Am J Gastroenterol.* 2007;102(8):1808-1825. **3.** Vakil N, Megraud F. Eradication therapy for Helicobacter pylori. *Gastroenterology.* 2007;133(3):985-1001. **4.** Graham-Lomax K, Graham DY. *Contemporary Diagnosis and Management of H pylori-Associated Gastrointestinal Diseases.* 3rd ed. Newtown, PA: Handbooks in Health Care Co; 2005. **5.** Vakil N, Fendrick AM. How to test for Helicobacter pylori in 2005. *Cleve Clin J Med.* 2005;72(suppl 2):S8-S13.

Otsuka
Medical Device Division of
Otsuka America Pharmaceutical, Inc.

BreathTek

August 2015 05US15EBP0047

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 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 (*p*UHR-CA), provided as a web-based calculation program, is required to obtain pediatric test results.

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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 heilmannii* or achlorhydria.
  - — Oral contamination associated with urease containing bacteria especially when not using the straw provided in the BreathTek UBT Kit.
- If particulate matter is visible in the reconstituted Pranactin-Citric solution after thorough mixing, the solution should not be used.
- Patients who are hypersensitive to mannitol, citric acid or Aspartame should avoid taking the drug solution as this drug 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.
- The safety of using the BreathTek UBT Kit during pregnancy and lactation is not established.
- For pediatric test results, the Urea Hydrolysis Rate (UHR) results must be calculated. Delta over Baseline (DOB) results in conjunction with the Pediatric Urea Hydrolysis Rate Calculation Application (*p*UHR-CA), provided as a web-based calculation program, is required to obtain pediatric test results. DOB results **cannot** be used to determine the infection status of pediatric patients. Use the web-based *p*UHR-CA (https://BreathTekKids.com) to calculate the UHR.
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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.

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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 each of cough, dry mouth and acute upper respiratory infection.

January 2016 05US16IBR0001

References: 1. Chey WD, Wong BCY; Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. *Am J Gastroenterol.* 2007;102(8):1808-1825. **2.** Talley NJ, Vakil NB, Moayyedi P. American Gastroenterological Association technical review on the evaluation of dyspepsia. *Gastroenterology.* 2005;129(5):1756-1780. **3.** Ables AZ, Simon I, Melton ER. Update on Helicobacter pylori treatment. *Am Fam Physician.* 2007;75(3):351-358. **4.** Malfertheiner P, Megraud F, O'Morain CA, et al; European Helicobacter Study Group. Management of Helicobacter pylori infection—the Maastricht IV/Florence Consensus Report. *Gut.* 2012;61(5):646-664. **5.** Fock KM, Katelaris P, Sugano K, et al; Second Asia-Pacific Conference. Second Asia-Pacific Consensus Guidelines for Helicobacter pylori infection. *J Gastroenterol Hepatol.* 2009;24(10):1587-1600. **6.** Koletzko S, Jones NL, Goodman KJ, et al; H. pylori Working Groups of ESPGHAN, NASPGHAN. Evidence-based guidelines from ESPGHAN and NASPGHAN for Helicobacter pylori infection in children. *J Pediatr Gastroenterol Nutr.* 2011;53(2):230-243.

Urea Breath Test for *H. pylori*

BreathTek®

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 dyspepsia†[1-5]
- UBT is also recommended to **confirm eradication in adults**[1,2,4,5] **and children**‡[6]

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.

*AAFP (2007),[3] ACG (2007),[1] AGA,[2] Maastricht/Florence Group IV (2010),[4] and Second Asia-Pacific Group (2009).[5]
†In adults under the age of 55 years and without alarm symptoms.[1]
‡North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN).

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Medical Device Division of
Otsuka America Pharmaceutical, Inc.

Urea Breath Test for *H. pylori*
BreathTek®

February 2016 05US16EBP0005

PAML
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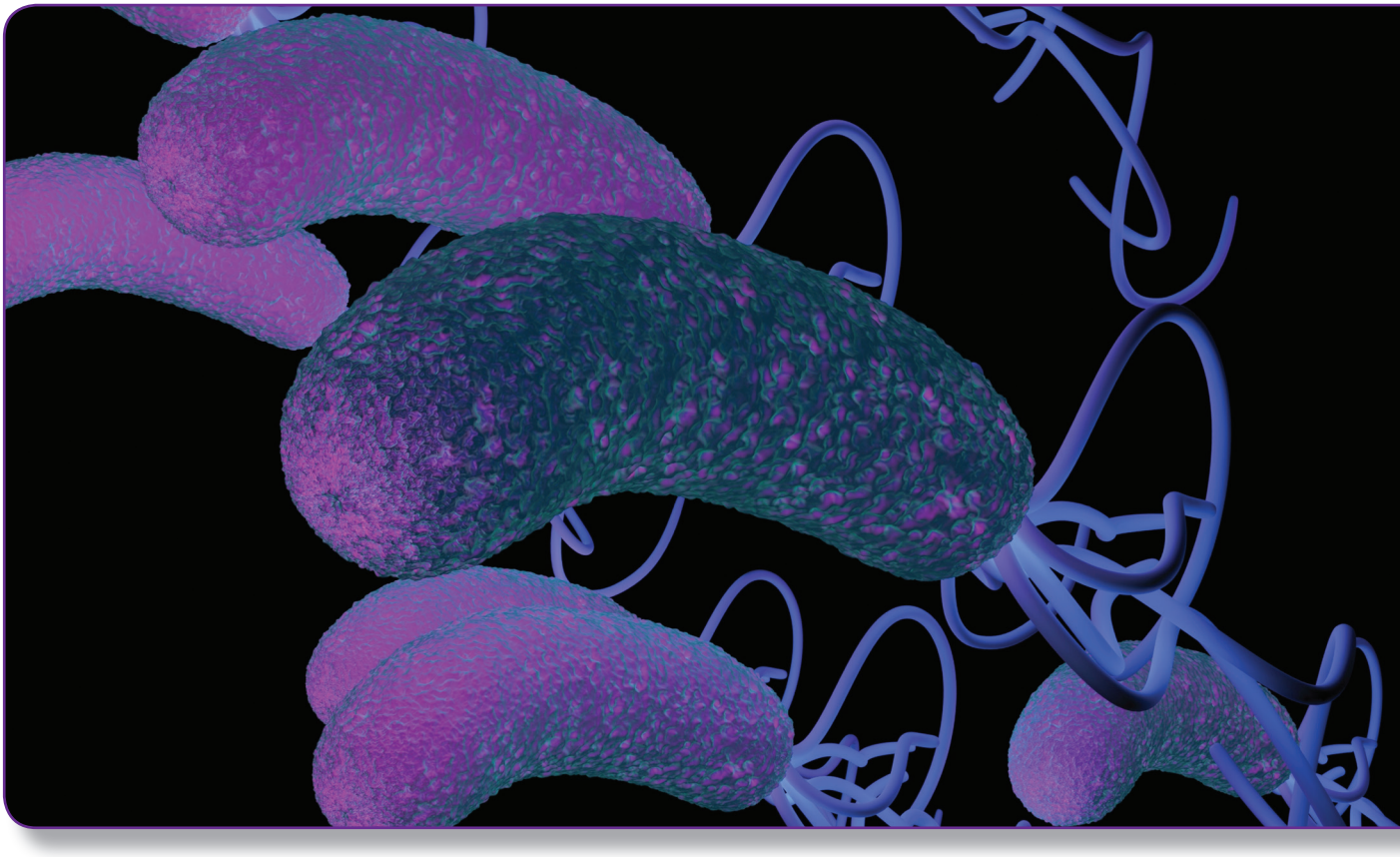
You suspect *H. pylori*



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.[6]
- *H. pylori* is a class-one carcinogen that greatly increases the risk of gastric cancer.[7]
- 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.

Management of Dyspepsia based on age and alarm features

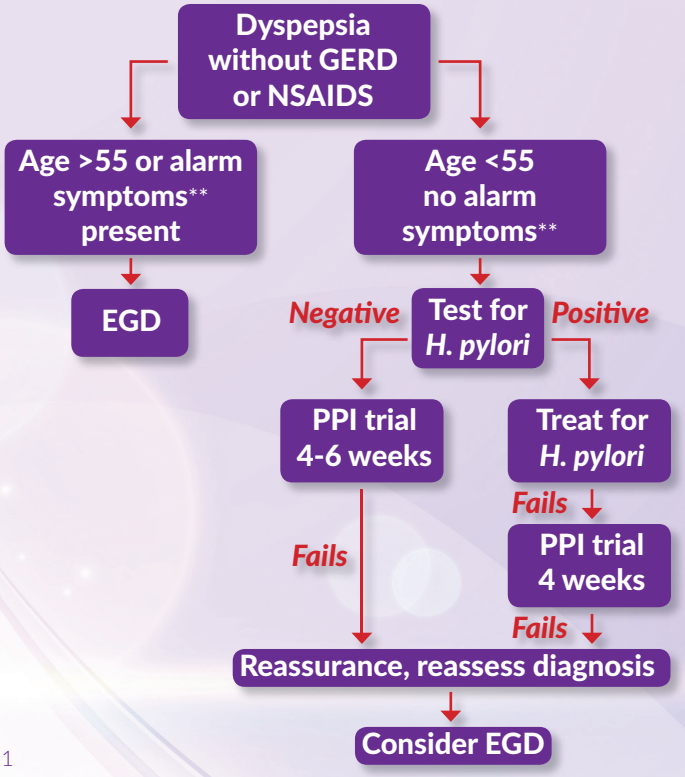


Figure 1

**Bleeding, anemia, early satiety, unexplained weight loss, progressive dysphagia, odynophagia, recurrent vomiting, family history of GI cancer, previous esophagogastric malignancy

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]

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]

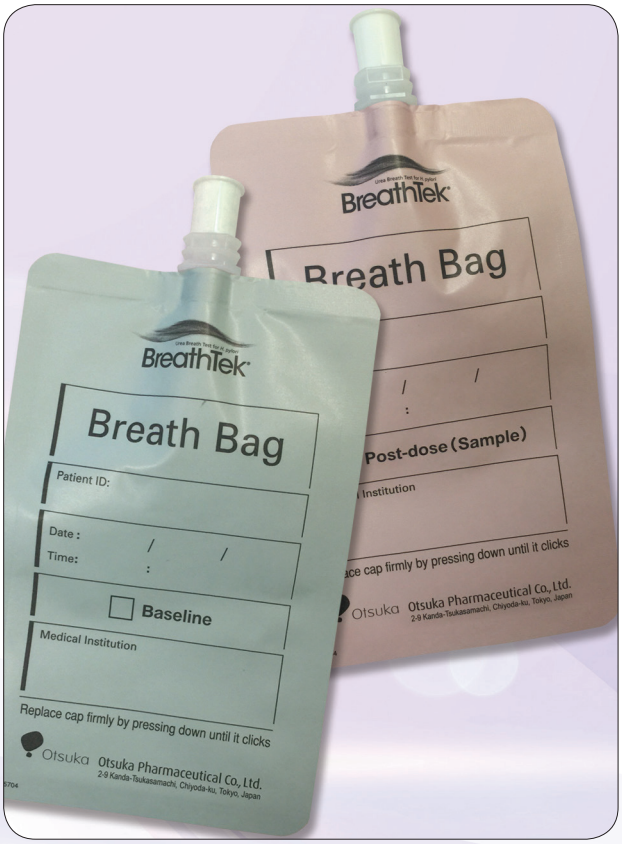
About 50% of patients with positive serology results do not have active *H. pylori* infections.[†]

- 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, anti-microbials, and bismuth 2 weeks prior to test.

HpSA®

- Stool collection at home
- No patient prep
- Suitable for all ages
- Discontinuing PPI's 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*.[8]

PAML
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*American College of Gastroenterology (ACG) and American Gastroenterological Association (AGA)
ł Assumes a 20% *H. pylori* prevalence rate.

References:

1. Chey WD, Wong BCY; Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Am J Gastroenterol. 2007;102(8):1808-1825.
2. Talley NJ, Vakil NB, Moayyedi P. American Gastroenterological Association technical review on the evaluation of dyspepsia. Gastroenterology. 2005;129(5):1756-1780.
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6. Hopkins RJ, et al, Relationship between Helicobacter pylori eradication and reduced duodenal and gastric ulcer recurrence: A review. Gastroenterology 1996; 110: 1244-1252.
7. Helicobacter Pylori Infection and Development of Gastric Cancer: Naomi Uemura, MD, et al, N Engl J Med; Vol. 345, No. 11, Sept. 13, 2001.
8. Fennerty B. Helicobacter pylori: why it still matters in 2005. Cleve Clin J Med. 2005;72(suppl 2):S1-S7

BreathTek® UBT for *H. pylori:*
Pediatric Use

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

BreathTek UBT 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

H. pylori is a common chronic infection affecting 1 in 4 children in the United States*[1]

- Transmitted predominantly among family members[2,3]
  - Highest rates of infection occur in children younger than 10 years of age[4]
- May become chronic without treatment[5]
- May cause duodenal ulcers, gastric ulcers, and progressive gastric mucosal damage in children[5-7]

Pediatric guidelines recommend the UBT method to confirm *H. pylori* eradication[8]

- 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]
- 94% of a joint NASPGHAN and ESPGHAN‡ panel strongly agreed that the ^{13}C-UBT is a reliable noninvasive test to determine *H. pylori* eradication[8]
- 9 in 10 declared serology is not reliable for use in the clinical setting[8]

*Data from the National Health and Nutrition Examination Survey (NHANES) III of children ages 6 to 19 years.
†North American Society for Pediatric Gastroenterology, Hepatology and Nutrition.
‡European Society of Paediatric Gastroenterology, Hepatology and Nutrition.

Please see accompanying BRIEF SUMMARY and enclosed Current Package Insert.

Urea Breath Test for H. pylori
BreathTek®

Diagnosing *H. pylori* in children

- In most children, *H. pylori* infection is not clinically apparent, even when causing chronic active gastritis[7]
- Children may present with gnawing or burning pain in the epigastrium, nausea, vomiting, or loss of appetite[6,10]
- Look for transmission between mother and child and siblings, which is most common. Another determinant is living in or originating from high-prevalence areas[2]

Confirming eradication is important because of:

- Poor compliance with medication[11]
- Reinfection as a result of intrafamilial transmission[11]
- Increasing antibiotic resistance[8]
  – In children treated with standard *H. pylori* therapy, eradication rates have been decreasing over time, in part because of increased antibiotic resistance[8]

BreathTek UBT: Convenient, reliable, noninvasive

BreathTek UBT delivers excellent sensitivity (96%) and specificity (99%) for diagnosing *H. pylori* in pediatric patients[12]

	AGE			ALL AGE GROUPS
	3–5 YEARS	6–12 YEARS	13–17 YEARS	COMBINED
SENSITIVITY	100%	100%	92%	96%
SPECIFICITY	100%	100%	98%	99%

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 heilmannii* or achlorhydria.

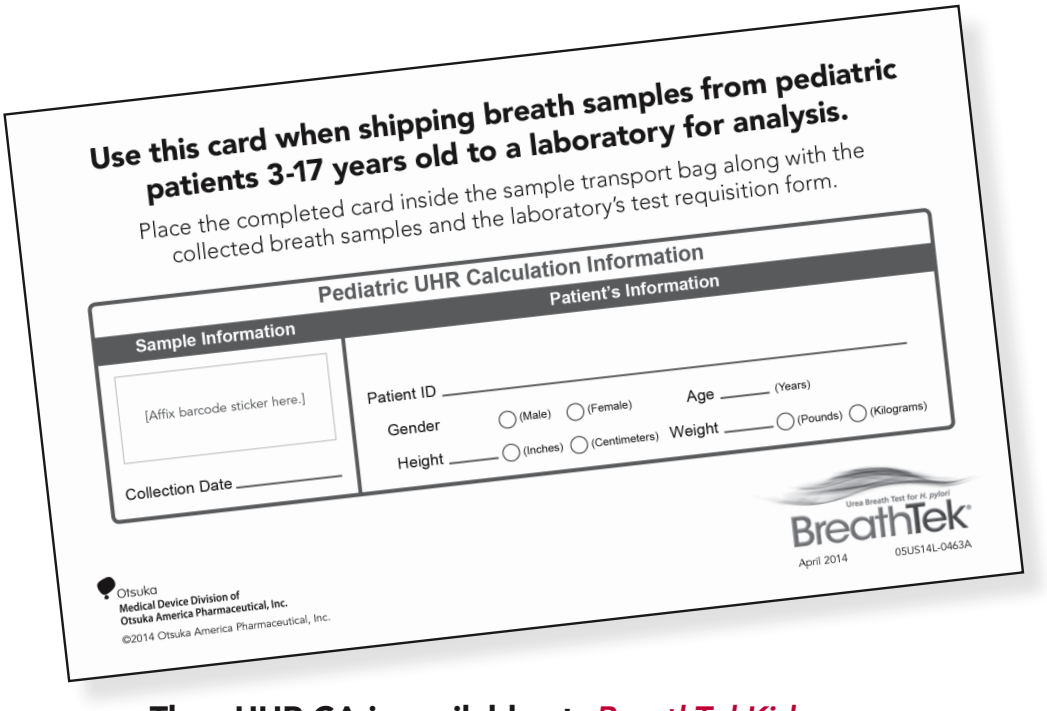
Please see accompanying BRIEF SUMMARY and enclosed Current Package Insert.

Using BreathTek UBT in children

Although the testing procedure will not change, the web-based Pediatric Urea Hydrolysis Rate Calculation Application (*p*UHR-CA) is needed to determine pediatric patient test results.

Steps for in-office sample collection and lab analysis:

1. Administer the test in your office as you would with adult patients.*
2. Complete the pediatric UHR card with the following information—which is needed so that the lab can perform the analysis and *p*UHR calculation:
   - Include collection date*, patient ID, gender, age, height, and weight
3. Enclose the card with the patient's sample.



The *p*UHR-CA is available at: *BreathTekKids.com*

When accessing the calculator for the first time, you will need to create an account.

Three available testing options for your convenience

IN OFFICE | IN LAB | IN OFFICE AND LAB

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

*Breath sample analysis must be performed within 7 days of breath sample collection.

Urea Breath Test for *H. pylori*
BreathTek®

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 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 (*p*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.

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, and should be used with caution in diabetic patients. (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 antimicrobials, or bismuth preparations within 2 weeks prior to performing the BreathTek UBT
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- Patients who are hypersensitive to mannitol, citric acid or Aspartame should avoid taking the drug solution as this drug 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.
- No information is available on use of the Pranactin-Citric solution during pregnancy.
- For pediatric test results, the Urea Hydrolysis Rate (UHR) results must be calculated. The Delta over Baseline (DOB) results are only used to calculate the UHR metrics to determine *H. pylori* infection in pediatric patients. DOB results **cannot** be used to determine the infection status of pediatric patients. Use the web-based *p*UHR-CA (https://BreathTekKids.com) to calculate the UHR.
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May 2014 05US14EBP1200

References: 1. Staat MA, Kruszon-Moran D, McQuillan GM, Kaslow RA. A population-based serologic survey of Helicobacter pylori infection in children and adolescents in the United States. *J Infect Dis.* 1996;174(5):1120-1123. **2.** Kivi M, Tindberg Y. Helicobacter pylori occurrence and transmission: a family affair? *Scand J Infect Dis.* 2006;38(6-7):407-417. **3.** Cervantes DT, Fischbach LA, Goodman KJ, Phillips CV, Chen S, Broussard CS. Exposure to Helicobacter pylori–positive siblings and persistence of Helicobacter pylori infection in early childhood. *J Pediatr Gastroenterol Nutr.* 2010;50(5):481-485. **4.** Malaty HM, El-Kasabany A, Graham DY, et al. Age at acquisition of Helicobacter pylori infection: a follow-up study from infancy to adulthood. *Lancet.* 2002;359(9310):931-935. **5.** Pacifico L, Anania C, Osborn JF, Ferraro F, Chiesa C. Consequences of Helicobacter pylori infection in children. *World J Gastroenterol.* 2010;16(41):5181-5194. **6.** Helicobacter pylori and peptic ulcer disease: the key to cure. Centers for Disease Control and Prevention website. http://www.cdc.gov/ulcer/keytocure.htm. Updated September 28, 2006. Accessed June 10, 2015. **7.** Gold B, Colletti R, Abbott M, et al. Helicobacter pylori infections in children: recommendations for diagnosis and treatment. *J Pediatr Gastroenterol Nutr.* 2000;31(5):490-497. **8.** Koletzko S, Jones NL, Goodman KJ, et al; H. pylori Working Groups of ESPGHAN and NASPGHAN. Evidence-based guidelines from ESPGHAN and NASPGHAN for Helicobacter pylori infection in children. *J Pediatr Gastroenterol Nutr.* 2011;53(2):230-243. **9.** Elitsur Y, Tolia V, Gilger MA, et al. Urea breath test in children: the United States prospective multicenter study. *Helicobacter.* 2009;14(2):134-140. **10.** Uc A, Chong SKF. Treatment of Helicobacter pylori gastritis improves dyspeptic symptoms in children. *J Pediatr Gastroenterol Nutr.* 2002;34(3):281-285. **11.** Moya DA, Crissinger KD. Helicobacter pylori persistence in children: distinguishing inadequate treatment, resistant organisms, and reinfection. *Curr Gastroenterol Rep.* 2012;14(3):236-242. **12.** Package Insert for BreathTek UBT. Otsuka America Pharmaceutical, Inc; 2014.

Learn more at BreathTek.com or call 888.637.3835.

Please see enclosed Current Package Insert.

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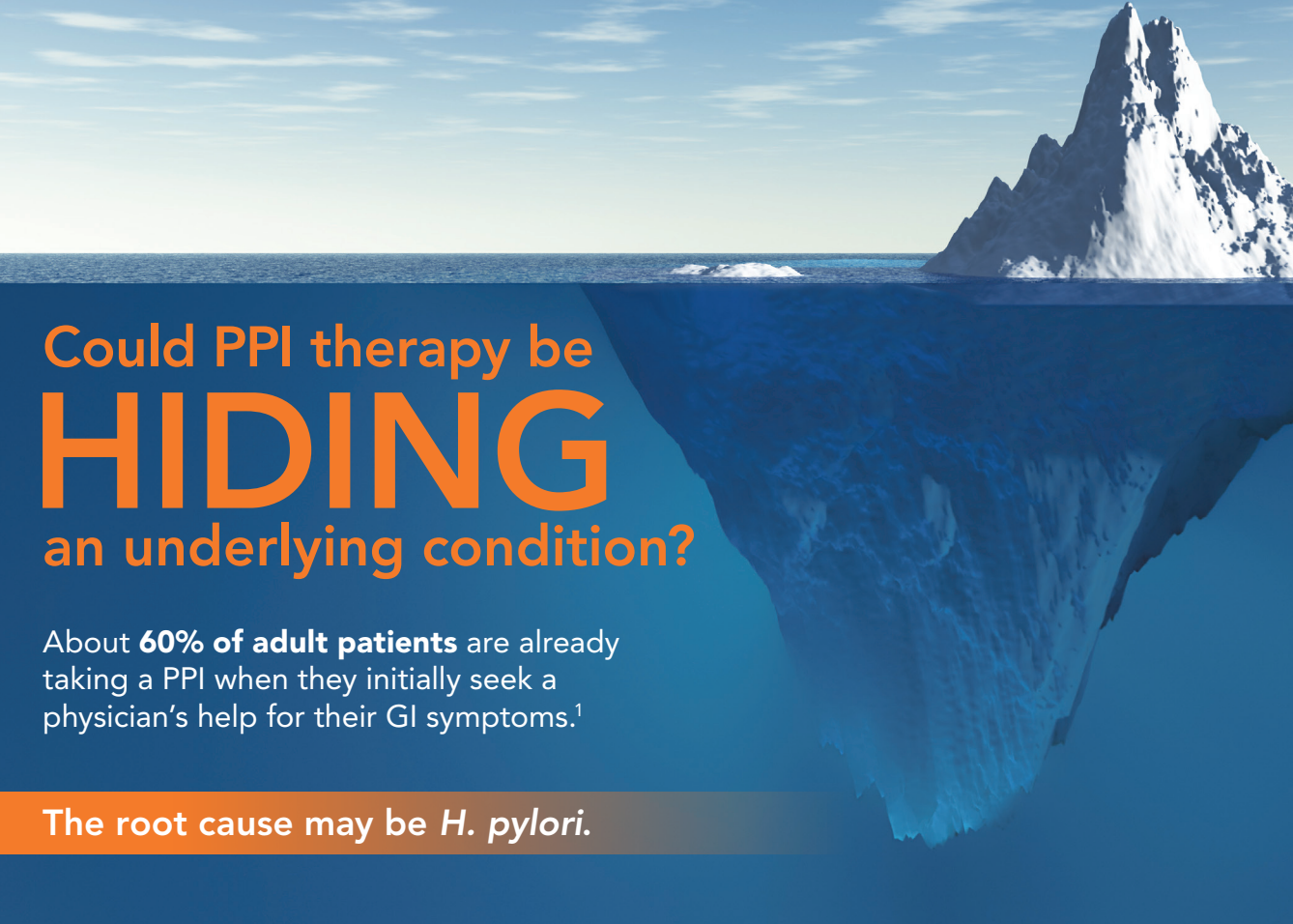
Medical Device Division of
Otsuka America Pharmaceutical, Inc.

Urea Breath Test for *H. pylori*
BreathTek®

June 2015 05US15EBP0034


Could PPI therapy be
HIDING
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.[1]
The root cause may be *H. pylori*.

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January 2016 05US16IBR0001

References: 1. Data on file. Otsuka America Pharmaceutical, Inc. **2.** Package Insert for BreathTek UBT. Otsuka America Pharmaceutical, Inc; 2016.

Urea Breath Test for *H. pylori*

BreathTek®

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[2]
- 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[2]
- The effect of histamine 2-receptor antagonists (H_2RAs) may reduce urease activity on urea breath tests. H_2RAs may be discontinued for 24 to 48 hours before the BreathTek UBT[2]
- The use of antacids does not appear to affect the accuracy of the BreathTek UBT[2]

Pooled data from 9 published studies of *H. pylori*–positive patients (N=626) confirm the performance of the UBT method in patients taking PPIs.[1]

Please see accompanying BRIEF SUMMARY and enclosed Current Package Insert.

Learn more at BreathTek.com or call 888.637.3835.

Otsuka
Medical Device Division of
Otsuka America Pharmaceutical, Inc.

Urea Breath Test for *H. pylori*
BreathTek®

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