Helicobacter Test **INFAI®**

$^{13}$C-urea breath test for *Helicobacter pylori* detection

*Helicobacter pylori* infection: A worldwide problem
**Facts**

**Helicobacter pylori infection**

A worldwide problem

On average, 50% of the world's population is already infected with *Helicobacter pylori*. Infection rates in Europe range from 35 - 40%.

*Helicobacter pylori* infection places the affected person under considerable physical and emotional strain. High economic costs lead to the necessity for eradication of the bacterium.

![Diagram showing the relationship between Helicobacter pylori infection and gastritis, dyspeptic complaints, duodenal and peptic ulcer, and carcinoma.]

- 50% *Helicobacter pylori* worldwide infection rate
- 100% detectable gastritis
- 30-40% dyspeptic complaints
- 10-15% duodenal and peptic ulcer
- Carcinoma?

**The most used 13C-urea breath test worldwide**

- Internationally approved medicinal product subject to medical prescription
- The best test for the diagnosis of *H. pylori* infection with high accuracy and easy performance (the Maastricht IV/ Florence Consensus Report)
- Suitable for diagnosis and control after eradication treatment of an infection with *H. pylori*
- Registered in more than 35 countries worldwide
- Reimbursement by health insurance in most European countries
- Easy handling, cost-effective and non-invasive
- Analysis via mass spectrometry or infrared spectroscopy
- The only approved 13C-urea breath test for children of the age 3 - 11
- NEW: CliniPac Basic (only 50 13C-urea containers) for general practitioner, laboratory and hospital use

**References**

- A new 13C-urea breath test to overcome false negative results to diagnose *H. pylori* infection in patients taking PPIs, Abstract P. Malfertheiner, EHSG, XVIII International Workshop Copenhague 2005.
- BSG Dyspepsia Management Guidelines (Guidelines in Gastroenterology, 2002).
- Validity of a novel biopsy urease test (HUT) and a simplified 13C-urea breath test for diagnosis of *H. pylori* infection and estimation of the severity of gastritis, Labenz J., Aygen S. and; Digestion, 1996, 57(6):391.
Performance of the test

Sampling of the 00-minute value $t_0$
Before performing the test, the patient should have fasted 4-6 hours, preferably overnight. The test starts with the collection of the baseline breath samples ($t_0$). The breath is collected either in a sampling tube (MS-version) or in a breath bag (IR-version) by gently blowing through a straw.

Administration of $^{13}$C-urea (test solution)
After drinking 200 ml of pure orange juice (100 ml of pure orange juice for children) or a solution of 1 g citric acid (for adults and adolescents) diluted in 200 ml of water to delay gastric emptying, the test solution is prepared. The enclosed $^{13}$C-urea (45 mg for children or 75 mg for adults and adolescents) is dissolved in 30 ml of water and taken immediately.

Sampling of the 30-minute value $t_{30}$
30 minutes after administration of the test solution, the second breath samples are collected ($t_{30}$). Barcoded labels are provided to ensure safe and distinctive identification during analysis. Breath samples should be dispatched to INFAI or other qualified laboratories in the box provided.

Basic principle

To establish an infection with *Helicobacter pylori*, $^{13}$C-labelled urea is administered which is then split up into $^{13}$C-labelled carbon dioxide and ammonia in the presence of the bacteria.

Quality criteria
Specificity of 98.5 % and sensitivity of 97.9 %.* Helicobacter Test INFAI® surpasses all other non-invasive diagnostic methods for *Helicobacter pylori* detection.

*European Medicines Agency: Summary of Product Characteristics Helicobacter Test INFAI®
Helicobacter Test INFAI® is safe, reliable, cost-saving, and can be performed easily and fast. The analysis of the breath samples can be carried out either by means of Isotope Ratio Mass Spectrometry (IRMS) or Non-Dispersive Infrared Spectroscopy (NDIR). For both analytical methods, the European Medicines Agency (EMA) approved specifications for their execution.

Analysis

Helicobacter Test INFAI® is regarded as proven if the difference in $^{13}\text{C}/^{12}\text{C}$ of 00-minute-value ($t_0$) and 30-minute-value ($t_{30}$) exceeds 4‰. An infection with Helicobacter pylori is regarded as proven if the difference in $^{13}\text{C}/^{12}\text{C}$ of 00-minute-value ($t_0$) and 30-minute-value ($t_{30}$) exceeds 4‰.
CLINICAL PARTICULARS: Therapeutic indications: Helicobacter pylori infection in adults and adolescents, who are likely to have peptic ulcer disease.

POSOLOGY AND METHOD OF ADMINISTRATION: This medicinal product should be administered by a healthcare professional and under appropriate medical supervision. Helicobacter Test INFAI is a breath test for single administration. Patients from the age of 12 must take the content of 1 jar with 75 mg. For performance of the test, 200 ml 100 % orange juice or 1 g citric acid in 200 ml water for patients from the age of 12 and older (as a pre-administered test meal), as well as tap water (for dissolving the 13C-urea powder) are necessary. The patient must have fasted for over 6 hours, preferably overnight. The test procedure takes approximately 40 minutes. In case it is necessary to repeat the test procedure, this should not be done until the following day. The suppression of Helicobacter pylori might give false negative results. Therefore the test shall be used at least after four weeks without systemic antibacterial therapy and two weeks after last dose of acid antisecretory agents. Both might interfere with the Helicobacter pylori status. This is especially important after Helicobacter eradication therapy. It is important to follow the instructions for use adequately, otherwise the reliability of the outcome will become questionable. CONTRAINDICATIONS: The test must not be used in patients with documented or suspected gastric infection or atrophic gastritis, which might interfere with the urea breath test. SPECIAL WARNINGS AND PRECAUTIONS FOR USE: A positive test alone does not constitute indication for eradication therapy. Differential diagnosis with invasive endoscopic methods might be indicated in order to examine the presence of any other complicating conditions, e.g. ulcer, autoimmune gastritis and malignancies. There is insufficient data on the diagnostic liability of the Helicobacter Test INFAI to recommend its use in patients with gastrectomy. For children from the age of 3, Helicobacter Test INFAI for children aged 3 to 11 is available. In individual cases of A-gastritis (atrophic gastritis) the breath test may have false positive results; other tests may be required to confirm the Helicobacter pylori status. If the patient vomits during the test procedure, necessitating the repetition of the test, this should be done in fasted condition and not before the following day. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION: Helicobacter Test INFAI will be affected by all treatments interfering with Helicobacter pylori status or urease activity. PREGNANCY AND LACTATION: It is not expected that the test procedure may be harmful during pregnancy or lactation. It is recommended to take notice of the product information of eradication therapy products for their use during pregnancy and lactation. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: Helicobacter Test INFAI has no influence on the ability to drive and use machines. UNDESIRABLE EFFECTS: Not known. OVERDOSAGE: Due to the fact that only 75 mg of 13C-urea is delivered, an overdose is not expected. LIST OF EXCIPIENTS: None. INCOMPATIBILITIES: Not applicable. SHELF-LIFE: 3 years. SPECIAL PRECAUTIONS FOR STORAGE: Do not store above +25°C.

MARKETING AUTHORIZATION HOLDER: INFAI Institut für biomedizinische Analytik und NMR-Imaging GmbH, Universitätsstraße 142, D-44799 Bochum, Germany. MARKETING AUTHORIZATION NUMBER: EU/1/97/045/001, EU/1/97/045/002, EU 1/97/045/004, EU/1/97/045/005. DATE OF REVISION OF THE TEXT: December, 2012

PHARMACEUTICAL FORM: Powder for oral solution.

CLINICAL PARTICULARS: Therapeutic indications: Helicobacter Test INFAI® for children aged 3 to 11 years will be affected by all treatments interfering with Helicobacter pylori status. If the patient vomits during the test procedure, necessitating the repetition of the test, this should be done in fasted condition and not before the following day. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION: Helicobacter Test INFAI® will be affected by all treatments interfering with Helicobacter pylori status or urease activity. PREGNANCY AND LACTATION: Not applicable. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: None. UNDESIRABLE EFFECTS: None known. OVERDOSAGE: Due to the fact that only 45 mg of 13C-urea is delivered, an overdose is not expected. LIST OF EXCIPIENTS: None. INCOMPATIBILITIES: Not applicable. SHELF-LIFE: 3 years. SPECIAL PRECAUTIONS FOR STORAGE: Do not store above +25°C.

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INFAI has established an integrated quality management system based on ISO 9001:2008, in compliance with national and international regulations. The high quality standards defined within this framework ensure the production of reliable and high-quality pharmaceutical products. Customer satisfaction is at the centre of all our activities. The permanent improvement of our quality management system enables us to act quickly upon changing market conditions.

The Company

Development and production of non-invasive methods for in vivo gastrointestinal diagnosis

INFAI is a research-based pharmaceutical company, offering new and innovative methods in the field of life science, as well as medicinal products, for the in vivo diagnosis of different widespread common diseases. These in vivo diagnostics are non-invasive and offer competitive advantages in comparison with other diagnostic tools.

In 1997, the $^{13}$C-urea breath test Helicobacter Test INFAI® was approved for all of Europe by the European Medicines Agency. Its use was subsequently extended to many other countries worldwide. Helicobacter Test INFAI® is now the most widely used test for the non-invasive diagnosis of infection with Helicobacter pylori.

In 1998, an automated production line was installed at our facility in Bochum, Germany, complying with all pharmaceutical quality guidelines. The production line was adapted in 2013 with new techniques conforming to the best state of pharmaceutical technology.

Additionally to Helicobacter Test INFAI®, the company is developing other innovative tests for the diagnosis of functional and metabolic disorders. These include:

- **Gastromotal®**: gastric emptying test (approval in progress)
- **Pancreo-Lip®**: test for slight to moderate degree of pancreatic insufficiency
- **Pancreo-Amyl®**: test for moderate to severe degree of pancreatic insufficiency
- **Lactoin®**: lactose intolerance test
- **Metabo Test®**: for congenital metabolic diseases (available)
- **Kidney function test**: for kidney insufficiency (available)

All tests were already used in several clinical trials worldwide.

Quality management

INFAI has established an integrated quality management system based on ISO 9001:2008, in compliance with national and international regulations. The high quality standards defined within this framework ensure the production of reliable and high-quality pharmaceutical products. Customer satisfaction is at the centre of all our activities. The permanent improvement of our quality management system enables us to act quickly upon changing market conditions.