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.

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

**One of 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 V - Florence Consensus Report)
- Suitable for diagnosis and control after eradication treatment of an infection with *H. pylori*
- Registered in more than 40 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: for patients with dyspepsia taking PPIs, INFAI offers the test with Refex® as a special test-meal, with just 1 day withdrawal of PPIs medication instead two weeks according Maastricht Guidelines (I, II, III, IV, V)
- NEW: CliniPac Basic (only 50 ¹³C-urea containers) for general practitioner, laboratory and hospital use

**References**

- Modified Helicobacter test using a new test meal and a ¹³C-urea breath test in Helicobacter pylori positive and negative dyspepsia patients on proton pump inhibitors. World J Gastroenterol 23 (2017) 5954-5961. Tepeš B., Malfertheiner P., Labenz J., Aygen S.
Performance of the test

**Sampling of the 00-minute value t₀**

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 (t₀). 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 ¹³C-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 ¹³C-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 t₃₀**

30 minutes after administration of the test solution, the second breath samples are collected (t₃₀). 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.

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**Basic principle**

To establish an infection with *Helicobacter pylori*, ¹³C-labelled urea is administered, which is then split up into ¹³C-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.

**References**

- 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.
An infection with *Helicobacter pylori* is regarded as proven if the difference in $^{13}$C/$^{12}$C of 00-minute-value ($t_0$) and 30-minute-value ($t_{30}$) exceeds 4‰.

Analysis

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.

Evaluation

![Graph showing the difference in $\Delta$δ ($^{13}$C/$^{12}$C) between 0 minutes and 30 minutes.](image)

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Helicobacter Test INFAI for adults and adolescents (mass spectrometry) EU/1/97/045/001

Helicobacter Test INFAI for children of the age 3-11 (mass spectrometry) EU/1/97/045/003

Helicobacter Test INFAI (infrared spectroscopy) EU/1/97/045/002

Helicobacter Test INFAI (infrared spectroscopy) EU/1/97/045/004

Helicobacter Test INFAI (infrared spectroscopy) Clnipac 50 (for 50 tests) EU/1/97/045/005

See Summary of Product Characteristics before prescribing.

PHARMACEUTICAL FORM: Powder for oral solution.

CLINICAL PARTICULARS: Therapeutic indications: Helicobacter Test INFAI may be used for in vivo diagnosis of gastroduodenal 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 after at least 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. 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. OVERDOSE: 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 GmbH, Gottfried-Hagen-Str. 60-62 D-51105 Cologne, 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, 2016.
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 13C-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 2017 new production line was installed at our facility in Hagen, Germany with new techniques conforming to the best state of pharmaceutical technology. In 2018 INFAI has furnished new packaging line and implemented the Falsified Medicines Directive.

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 -
- *Cardio Test INFAI®* - for cardio risk assessment - available -

All tests were already used in several clinical trials worldwide.

Quality management

INFAI has established an integrated quality management system based on ISO 9001:2015, 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.