Helicobacter Test *INFAI*®

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

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

Helicobacter Test *INFAI*®

Facts

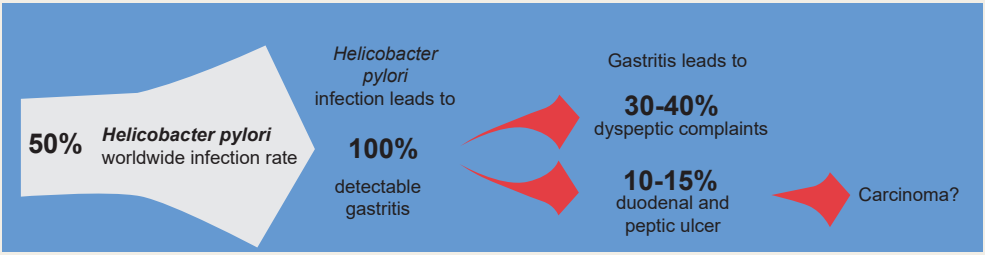
Helicobacter pylori infection

A worldwide problem

On average, 50 % of the world‘s population is already infected with *Helicoba cter 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.



One of the most used ^{13}C-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 ^{13}C-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 ^{13}C-urea containers) for general practitioner, laboratory and hospital use

References

- Management of Helicobacter pylori infection-the Maastricht V/ Florence Consensus Report. Gut, 2017; 66:(1). P Malfertheiner, F Megraud, C A O`Morain, et.al.
- Modified Helicobacter test using a new test meal and a ^{13}C-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.
- The Helicobacter Eradication Aspirin Trial (HEAT): A Large Simple Randomised Controlled Trial Using Novel Methodology in Primary Care. EBioMedicine 2 (2015) 1200-1204. Jennifer S. Dumbleton, Anthony J. Avery, Carol Coupland, et. al.
- Evaluation and Management of dyspepsia. Harmon RC, Peura DA. Therap Adv Gastroenterol. 2010 Mar;3(2):87-98.
- A method of the diagnosis of H. Pylori infection and diagnostic kit for performing the method. Aygen S.; 2009, EP 1 685 851 B1.
- Epidemiology of Helicobacter pylori Infection in the Czech Republic. 2015 Helicobacter 11: 56-65.Jan Bureš, Marcela Kopáčová, Iona Koupil, et. al.

Helicobacter Test *INFAI*®

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.

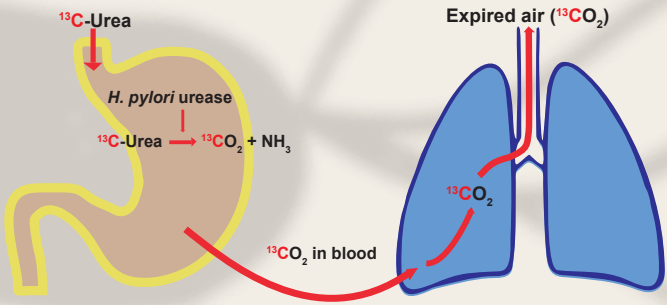
Administration of ^{13}C-urea (test solution)

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

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

References

- Comparison of non-invasive tests to detect Helicobacter pylori infection in children and adolescents: Results of a multicenter European study. Mégraud, F. et al.; J. Pediatrics, 2005, 146 (2):198.
- Utility and acceptability of INFAI ^{13}C-urea breath test. Alberti H. et al.; BMJ, 2002, 324: 485.
- Validity of a novel biopsy urease test (HUT) and a simplified ^{13}C-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.

Helicobacter Test *INFAI*®

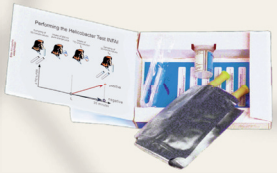
Analysis

Analysis of the breath test

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.

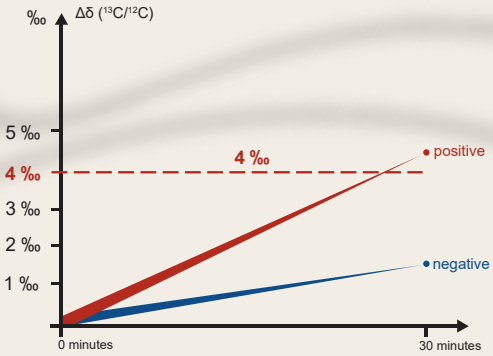
Test kit for Mass Spectrometry

or



Test kit for Infrared Spectroscopy

Evaluation



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‰.

Helicobacter Test *INFAI*®

Products

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

Helicobacter Test *INFAI*
for adults and adolescents
(infrared spectroscopy)
EU/1/97/045/002

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

Helicobacter Test *INFAI*
Clinipac 50 (for 50 tests)
(infrared spectroscopy)
EU/1/97/045/004

Helicobacter Test *INFAI*
CliniPac Basic (only 50 ^{13}C-urea containers)
Applicable for mass spectrometry or infrared spectroscopy
EU/1/97/045/005

Helicobacter Test INFAI for adults and adolescents (for mass spectrometry, for infrared spectroscopy), Clinipac 50 for 50 tests and CliniPac Basic.

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 ^{13}C-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, 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. OVERDOSE: Due to the fact that only 75 mg of ^{13}C-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 AUTHORISATION HOLDER: INFAI GmbH, Gottfried-Hagen-Str. 60-62 D-51105 Cologne, Germany.
MARKETING AUTHORISATION NUMBER:
EU/1/97/045/001, EU1/97/045/002,EU 1/97/045/004, EU/1/97/045/005.
DATE OF REVISION OF THE TEXT: December, 2016

Helicobacter Test INFAI for children of the age 3 to 11.

See Summary of Product Characteristics before prescribing.

PHARMACEUTICAL FORM: Powder for oral solution.
CLINICAL PARTICULARS: Therapeutic indications: Helicobacter Test INFAI for children aged 3 to 11 years may be used for in vivo diagnosis of gastroduodenal *Helicobacter pylori* infection: for the evalutation of the success of eradication treatment, or, when invasive tests cannot be performed, or when there are discordant results arising from invasive tests. This medicinal product is for diagnostic use only.
POSOLOGY AND METHOD OF ADMINISTRATION: This medicinal product should be administered by a healthcare professional and under appropriate medical supervision. Helicobacter Test INFAI for children aged 3 to 11 years is a breath test for single administration. Children from the aged of 3 to 11 years must take the content of 1 jar with 45 mg. For performance of the test, 100 ml 100 % orange juice for patients from the age of 3 to 11 (as a pre-administered test meal), as well as tap water (for dissolving the ^{13}C-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, 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 for children aged 3 to 11 years to recommend its use in patients with gastrectomy and in patients younger than 3 years of age. 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 for children aged 3 to 11 years 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. OVERDOSE: Due to the fact that only 45 mg of ^{13}C-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 AUTHORISATION HOLDER: INFAI GmbH, Gottfried-Hagen-Str. 60-62, D-51105 Cologne, Germany.
MARKETING AUTHORISATION NUMBER: EU/1/97/045/003.
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Helicobacter Test *INFAI*®

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Our local representatives can be found on www.infai.de

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 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 Helicbacter Test *INFAI*, the company is developing other innovative tests for the diagnosis of functional and metabolic disorders. These inculde:

- **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 assesment- **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.

QUALITY SYSTEM CERTIFICATION
DNV·GL
ISO 9001

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