C-13 UREA

Prescribing Information

1 NAME OF THE MEDICINAL PRODUCT

C-13 UREA

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 75mg of ^{13}C-Urea

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

C-13 UREA 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.

4.2 Posology and Method of Administration

This medicinal product should be administered by a healthcare professional and under appropriate medical supervision.

The diagnostic drug component of the test kit is ^{13}C-enriched urea in the form of a tablet. One tablet should be used for each test.

Refer to ‘Instructions for use and handling’ (section 6.6) and the instructions for use (IFU) provided with the kit.

The test kit is intended for single patient use only.

Patient Preparation

The patient should fast at least one hour before administering the solution.

The patient should not take antimicrobials, proton pump inhibitors (PPI) or bismuth preparations within two weeks prior to administering the test. If PPIs are used within two weeks of breath testing, false negative test results may occur, and the test should be repeated two weeks after discontinuation of PPI treatment. A positive result for a patient on PPI could be considered as indicative of the presence of urease enzyme associated with *H. pylori*.

Pediatric Use

Safety and efficacy in patients under the age of 18 years have not been established.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

The patient should not take antimicrobials, proton pump inhibitors (PPI) or bismuth preparations within two weeks prior to administering the test.

4.4 Special Warnings and Precautions for Use

For in vitro diagnostic use only. The C-13 UREA tablet and Citrica powder are dissolved in a glass of water, and the resulting solution is taken orally as part of the diagnostic procedure. When orange juice is used, the tablet should be dissolved in the orange juice.

1. Phenylketonurics: remind the patient that the Citrica powder (see section 6.6) contains 84 mg Phenylalanine. Phenylketonurics restrict dietary intake of phenylalanine.

2. A negative result does not rule out the possibility of *H. pylori* infection. False negative results can occur with this procedure. If clinical signs suggest *H. pylori* infection, retest with a new sample or an alternate method.

3. A false positive test may occur due to urease associated with other gastric spiral organisms observed in humans such as *Helicobacter heilmanni*.

4. A false positive test could occur in patients who have achlorhydria.

5. False negative test results may be caused by:

- Ingestion of antimicrobials or bismuth preparations within two weeks prior to performing the breath test.
- Ingestion of proton pump inhibitors (PPIs) within two weeks prior to performing the breath test.

Note: If a negative result is obtained from a patient ingesting a PPI within two weeks prior to the breath test, the results cannot be considered indicative of the absence of urease associated with *H. pylori* and the test should be repeated two weeks after discontinuing the PPI treatment. A positive result for a patient on a PPI could be considered as indicative of the presence of urease associated with *H. pylori*.

6. Data is insufficient for recommending the use of this test on patients with total or partial gastrectomy.

7. A correlation between the number of *H. pylori* organisms in the stomach and the breath test results has not been established.

8. Post treatment monitoring of *H. pylori* should be performed after at least six weeks of treatment for *H. pylori* infection. Earlier assessment may give false results.

4.5 Interaction with other medicinal products and other forms of interaction

Potentially interfering substances typically found in a patient's breath were tested to determine their effect on the test results. The potential sources tested were:

- Mouthwash
- Chewing gum
- Carbonated beverages
- Cigarette smoke
- Acetone (to simulate the effect of ketone production that may result from some diets)
- Alcohol

There was no observation that these substances had any significant influence on the outcome of the test.

4.6 Fertility, Pregnancy and Lactation

Data is insufficient to recommend the use of this test on pregnant and lactating women.

4.7 Effects on ability to drive and use machines

Studies to determine the effect of C-13 Urea tablet on the ability to drive and use machines have not been conducted.

4.8 Undesirable effects

The adverse events seen with the test solution are generally mild and transient. The following rare adverse events have been identified: anaphylactic reaction, diarrhea and vomiting. 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 465 patients of at least 18 years-old and older to determine the initial diagnosis and post treatment monitoring of *H. pylori* infection using the kit, the following adverse events experienced by 1.5% of these patients were nausea (0.6%), throat burning (0.4%) and lightheadedness (0.4%). The last one was reported after collecting the breath samples. The potential adverse events were experienced by the patients within minutes of ingestion of the Urea C-13 tablet and Citrica powder.

<u>Reporting of suspected adverse reactions</u>

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il

4.9 Overdose

In the case of accidental overdose – drink water and call the physician.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other diagnostic agents

ATC Code: V04CX

Mechanism of Action

The C-13 UREA tablet is part of a breath test kit. The breath test is a diagnostic test that analyzes a breath sample before and after ingestion of ^{13}C-enriched urea; it is used to identify those patients with *H. pylori* infection.

The breath test is performed as follows: a 75mg C-13 UREA tablet and 4.3g Citrica powder are dissolved in water. When orange juice is used, the tablet is dissolved in it. The resulting solution is ingested by the patient. The presence of Citrica or orange juice creates an acidic environment in the stomach and delays the transfer of the ingested solution to the duodenum. These two characteristics facilitate the decomposition of the urea by *H. pylori*, if present. Thus, in the presence of urease associated with gastric *H. pylori*, ^{13}C-Urea is decomposed to $^{13}CO_2$ and NH_3 according to the following equation:

$$^{13}\text{C-Urea} + H_2O \xrightarrow{\textit{H. pylori}\ \text{urease}} {}^{13}CO_2 + 2\ NH_3$$

The $^{13}CO_2$ is absorbed into the blood and then exhaled in breath. Absorption and distribution of $^{13}CO_2$ is fast. Therefore, the cleavage of urea by the *H. pylori* urease that produces the $^{13}CO_2$ occurs immediately after the solution is ingested and enables immediate detection of increased $^{13}CO_2$ in the exhaled breath of *H. pylori*-positive patients. In the case of *H. pylori*-negative patients, the ^{13}C-Urea does not produce $^{13}CO_2$ in the stomach because there are no human enzymes that can decompose the urea in the stomach.

5.2 Pharmacokinetic Properties

The orally applied ^{13}C-Urea is metabolized to carbon dioxide and ammonia or is integrated into the body's own urea cycle. Any increase in $^{13}CO_2$ will be measured by isotopic analysis.

Absorption and distribution of $^{13}CO_2$ is faster than the urease reaction. Therefore, the rate-limiting step in the whole process is the cleavage of ^{13}C-Ureaby Helicobacter's urease.

Only in *Helicobacter pylori*-positive patients does the administration of 75 mg labelled urea lead to a significant increase of $^{13}CO_2$ in the breath sample within the first 20 minutes.

5.3 Preclinical Safety Data

No concerns in relation to the clinical use of the product.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sodium Benzoate, Povidone, Microcrystalline Cellulose, Colloidal Silicon Dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Each aluminum sachet contains one tablet. The sachet is part of a kit. The kit also contains 2 test tubes: 'BEFORE' (labeled as 00 MINS) and 'AFTER' (labeled as 20 MINS), 2 straws, citric acid powder called Citrica (contains phenylalanine) and an IFU.

6.6 Instructions for use and handling

The test is to be performed in the presence of a qualified person.

Preparation of the test drink:

Dissolve the C-13 UREA tablet in 150–200 mL of room-temperature water (do not use hot or cold water). Add the citric acid powder ("Citrica"), provided in a separate sealed pouch, to the same cup.

- Stir thoroughly with the provided straw for 2 to 3 minutes until the Citrica powder and the C-13 UREA tablet are completely dissolved. However, tiny particles might still be seen in the test drink after stirring.
- Alternatively, the tablet may be dissolved in 150 to 200 ml of orange juice without Citrica.
- The contents of the test drink should be consumed through a straw within two minutes of *preparation*.

Note:

If substantial particles are still present after 5 *minutes of stirring, discard the* test drink *and repeat the procedure with* a *new kit, which contains a new tablet.*

Administer the test drink within two hours of preparation, as this is the maximal time to maintain solution stability.

7 DRUG REGISTRATION NUMBER

130-45-30942-02

8 LICENSE HOLDER

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Approved in December 2025 according to MOH’s guidelines.