SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Espikur 50 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet contains 50 mg of ^{13}C Urea.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet
White, round convex tablet, 12 mm in diameter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For *In vivo* diagnosis of primary or remaining gastroduodenal *Helicobacter pylori* infection in adults.
This medicinal product is for diagnostic use only.

4.2 Posology and method of administration

Posology
Espikur 50 mg tablet is a breath test for single administration. One tablet as a single dose at one test occasion.

Method of administration
Espikur tablet is for oral administration. The patient should fast for at least six hours before the test. The test procedure takes approximately 10 minutes. A baseline breath sample is collected after which the tablet is swallowed whole with a glass of water. Ten minutes later, a second breath sample will be collected.
If the patient chews the tablet, the test must be performed again as the risk of false positive results increase. A new test may thus be performed 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 (see section 4.5).It is important to follow the instructions for use, described in section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
The test must not be used due to false results, in patients with:

- documented or suspected gastric infection
- atrophic gastritis

4.4 Special warnings and precautions for use

Espikur 50 mg tablet is an *in vivo* diagnosis of gastroduodenal *Helicobacter pylori* infection. It cannot prejudge the pathology associated with *Helicobacter pylori* infection. Alternative diagnosis with other methods might be indicated in order to examine the presence of any other complicating conditions, eg. gastric ulcer, autoimmune gastritis and malignancies.

There is insufficient data on the diagnostic liability of the Espikur 50 mg tablet to recommend its use in patients with partial or total gastrectomy.

There are insufficient data to recommend the use of Espikur 50 mg tablet in patients younger than 18 years.

4.5 Interaction with other medicinal products and other forms of interaction

The validity of the test result may be affected if the patient is currently being treated with antibiotics or a proton-pump inhibitor or has just completed a course of treatment with these drugs. The results may be affected in general by all treatments interfering with *Helicobacter pylori* status or urease activity.

Suppression of *Helicobacter pylori* may lead to false negative results. Therefore, the test shall be used after at least four (4) weeks without systemic antibacterial therapy and at least two (2) weeks after last dose of acid antisecretory agents. This is particularly important after *Helicobacter pylori* eradication therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy and breastfeeding
The endogenous production of urea amounts to 25 – 35 g/day. It is therefore unlikely that the dose of 50 mg urea should cause any adverse effects on pregnancy and lactation.

The Espikur test is not expected to be harmful during pregnancy or to the health of the foetus/newborn child. Espikur can be used during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

Espikur has no or negligible influence on the ability to drive or to use machines.

4.8 Undesirable effects

Adverse reactions are listed by MedDRA body system organ class and by frequency (Very common (≥1/10); common (≥1/100 to < 1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000))

Gastrointestinal disorders
Very rare: stomach pain
General disorders and administration site conditions
Very rare: fatigue
Nervous system disorders
Very rare: parosmia

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V*.

4.9 Overdose

Overdose is unlikely to occur in the intended clinical circumstances. No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other diagnostic agents, ATC code: V04CX05

Mechanism of action

After oral ingestion, labelled urea tablet reaches the stomach, where it disintegrates rapidly. In the case of infection with *Helicobacter pylori*, ^{13}C-urea is metabolised by the enzyme urease of *Helicobacter pylori*.

$$H_2N(^{13}CO)\,NH_2 + H_2O \xrightarrow{\text{Enzyme urease}} 2NH_3 + {}^{13}CO_2$$

The labelled carbon dioxide diffuses into the blood vessels and is transported as bicarbonate to the lungs where it is then liberated as $^{13}CO_2$ in exhaled air.
Infection with *Helicobacter pylori* will significantly change the $^{13}C/^{12}C$ – carbon isotope ratio. This ratio change (increases) in a post-urea breath sample compared to baseline breath sample taken before urea intake.

The proportion of $^{13}CO_2$ in the breath samples is determined by isotope-ratio-mass spectrometry (IRMS) or by another suitably-validated method carried out by any qualified laboratory, and stated as an absolute difference (Δδ-value) in the value between a pre-urea (00-minute value) and post-urea breath sample (10-minute value; see section 6.6).

The cut off point for discriminating between *H. pylori* positive and negative patients is based on a study with 885 patients. Values below 1.5‰, i.e. ≤1.5‰ are diagnosed as negative and values above i.e. >1.5‰ are diagnosed as positive.

In order to determine test performance and to fulfil lack of direct comparison vs Standard of Truth (SoT) at the registered dose, a simulation analysis was carried out based on two comparative studies: the **sensitivity** was 94.3% (95% CI = [85.1% -98.5%]) and **specificity** was 97.1% (95% CI = [92.4% - 99.2%]). The **accuracy** was 96.2% (95% CI = [92.2-98.5%]) and with the **PPV** (positive predicted value) of 94.0% (95% CI = [84.6-98.3%]) and **NPV** (negative predicted value) 97.3% (95% CI = [92.7-99.3%]).

5.2 Pharmacokinetic properties

Absorption
Urea is rapidly absorbed from the gastro-intestinal tract.

Distribution
Urea is distributed into extracellular and intracellular fluids including lymph, bile, cerebrospinal fluid and blood. It is reported to cross the placenta and penetrate the eye.

Elimination
Urea is excreted unchanged in the urine.

5.3 Preclinical safety data

Non-clinical data reveal no concerns of relevance for the clinical use of the product.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric Acid, Anhydrous
Silica, Colloidal Anhydrous
Croscarmellose Sodium
Microcrystalline Cellulose
Magnesium Stearate
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package in order to protect from light.

6.5 Nature and contents of container

1 tablet in aluminium blister (with sample tubes and disposable straw)
10 x 1 tablets in aluminium blister (without sample tubes and disposable straw).
Not all pack sizes may be marketed.
Breath bags are provided separately.

Component	1 tablet (kit)	10 x 1 tablet
Tablet in an aluminium blister	1	10
Sample tubes for 00-minute breath sample (blue stopper)	2	-
Sample tubes for 10-minute breath sample (red stopper)	2	-
Disposable straw	1	-
Package leaflet	1	1
Barcode labels for the sample tubes	4	-
Extra barcode labels	2	-

6.6 Special precautions for disposal and other handling

It is recommended to perform the test with the patient being in a resting position.

If the test is to be carried out in the morning, the patient should fast overnight and not eat breakfast. If the test is to be carried out later in the day, or if fasting may cause some problems for the patient, then

only a light breakfast, e.g. tea and toast, is allowed. Also, if the patient has eaten a heavy meal then it will be necessary to fast for six hours prior to the test.
The collection of breath samples can be performed using tubes or breath bags.

Stepwise description of the test procedure using sample tubes

To perform the test, 4 sample tubes with stoppers and 1 straw are provided.

Keep one of the extra bar code labels as a reference label for the patient's journal.

1. The patient should begin the procedure with the two 00-MINUTES sample tubes with blue stopper
   - Unscrew the stopper
   - Place the straw in the bottom of the sample tube
   - Take a deep breath and exhale gently into the tube
   - Remove the straw from the tube and close the tube with the stopper immediately.
   - Check that the stopper is properly closed.
   - Repeat the test with the second 00-MINUTES sample tube
2. Swallow the tablet with a glass of water. Wait for 10 minutes in an upright position (standing or sitting position).
3. Exhale into the two 10-MINUTES tubes with red stopper in the same way as described above.

After the collection of samples, the 4 tubes should be labelled as per the image below, with one barcode label being placed lengthways on each tube.

The 4 labelled sample tubes should be forwarded for analysis to the local diagnostic laboratory.

Handle the sampled tubes with care and avoid any damage which may cause leakage.

Stepwise description of the test procedure using breath bags

To perform the test, 2 single breath bags or 1 double bag and 1 mouth piece are used.

1. Remove the stopper cap from the breath bag hose and connect a mouth piece to the hose. The patient should exhale through the mouth piece for the baseline (00-MINUTE) breath bag sample. Remove the mouth piece from the breath bag and close the breath bag with the stopper cap.
2. Swallow the tablet with a glass of water. Wait for 10 minutes in an upright position (standing or sitting position)
3. Exhale into the unused side of the double breath bag or to another single breath bag for the test (10-MINUTES) breath bag sample in the same way as described above.

Mark the breath bags in order to identify the different samples (e.g."zero test" and "10 min test").
Handle the sampled breath bags with care and avoid any damage which may cause leakage.

Analysis of breath samples

It has to be ensured that the analysis is carried out by an approved and certified laboratory. Laboratories and analysis equipment used should comply with EU directives. This directive implies that the analysis equipment should be CE marked and approved for analysis of breath tests.
Breath samples, can be analysed by isotope-ratio-mass spectrometry IRMS or by another suitably-validated method and carried out by a qualified laboratory.

Explanation of analysis results

Δ δ-value;
The difference in parts per thousand (‰) between the 00-MINUTE value and the 10 MINUTE value.
Helicobacter pylori status:
≤1.5 ‰ Δ δ-value = Negative *Helicobacter pylori* status.
>1.5 ‰ Δ δ-value = Positive *Helicobacter pylori* status.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Laboratoires MAYOLY SPINDLER
3 Place Renault
92500 Rueil Malmaison
France

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

{MM/YYYY}

10. DATE OF REVISION OF THE TEXT

2 October 2025

Detailed information on this medicinal product is available on the website of name of {MS/Agency}.