

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE MEDICINAL PRODUCT

Pylobactell, 100 mg, Soluble Tablet

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance	Quantity per tablet
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<sup>13</sup> C-urea	100 mg
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For excipients, see 6.1

**DRUGS-ABOUT.COM**

## 3. PHARMACEUTICAL FORM

Soluble tablet

A white, biconvex tablet.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

For *in vivo* diagnosis of gastroduodenal *Helicobacter pylori* infection.

### 4.2 Posology and method of administration

The Pylobactell tablet is for oral administration.

*Adults* : The tablet is to be dissolved in water and taken 10 minutes after the start of the breath test procedure.

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 is a problem for the patient, then a light breakfast only, eg. tea and toast, is recommended. If the patient has eaten a heavy meal then it will be necessary to fast for six hours prior to the test.

It is important to follow the instructions for use described in Section 6.6 adequately, otherwise the validity of the test result will be questionable.

### 4.3 Contra-indications

The test must not be used in patients with documented or suspected gastric infection that might interfere with the urea breath test.

Hypersensitivity to the active substance or to any of the excipients.

### 4.4 Special warnings and special precautions for use

A positive urea breath test alone does not clinically confirm that eradication therapy is indicated.

Alternative diagnosis with invasive endoscopic methods might be indicated in order to examine the presence of any other complicating conditions, eg. gastric ulcer, autoimmune gastritis and malignancies.

In individual cases of atrophic gastritis, the breath test result may have a false positive outcome and other tests may be required to confirm the presence of *H.pylori*.

If a repeat test is required, it should not be carried out until the following day.  
For patients who do not tolerate the recommended test meal, an alternative test meal should be given.  
Care should be taken in patients where fasting may have medical implications.

There are insufficient data on the diagnostic reliability of the Pylobactell test to recommend its use in patients with partial gastrectomy and 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 completed a course of treatment with these drugs. The results may be affected in general by all treatments interfering with *H.pylori* status or urease activity.

Suppression of *H. pylori* might give false negative results. Therefore, the test must not be used until four weeks without systemic antibacterial therapy and two weeks after last dose of acid antisecretory agents. This is especially important after eradication therapy.

#### **4.6 Pregnancy and lactation**

The endogenous production of urea amounts to 25 - 35 g/day. It is therefore unlikely that the dose of 100 mg urea should cause any adverse effect on pregnancy and lactation.

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

#### **4.7 Effects on ability to drive and use machines**

Not relevant.

#### **4.8 Undesirable effects**

None known.

#### **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 : V04C X.

In the case of infection with *H.pylori*, orally ingested <sup>13</sup>C-urea is metabolised by the enzyme urease which is present in *H.pylori*.



The carbon dioxide which is liberated diffuses into the blood vessels and is transported as bicarbonate to the lungs where it is then liberated as  $^{13}\text{CO}_2$  in exhaled air. Infection with *H.pylori* will significantly change the  $^{13}\text{C}/^{12}\text{C}$  - carbon isotope ratio.

The proportion of  $^{13}\text{CO}_2$  in the breath samples may be 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 (excess) in the value between the pre-urea and post-urea breath samples (see Section 6.6).

The cut off point for discriminating between *H.pylori* negative and positive patients is set to an excess value of 3.5, i.e.  $<3.5$  is negative and  $\geq 3.5$  is positive.

In comparison with biopsy based techniques for diagnosing *H.pylori* infection, using data from two therapeutic trials, Pylobactell achieved during different conditions (prestudy and follow-up visits) sensitivity estimates above 95 % with lower one-sided 95 % confidence limit ranging from 93 % to 98 %. The specificity estimates were all above 90 % with corresponding lower confidence limits ranging from 85 % to 90 %.

## **5.2 Pharmacokinetic properties**

Urea is rapidly absorbed from the gastro-intestinal tract and distributed into extracellular and intracellular fluids including lymph, bile, cerebrospinal fluid and blood. It is reported to cross the placenta and penetrate the eye. It is excreted unchanged in the urine.

## **5.3 Preclinical safety data**

There are no concerns in relation to the clinical use of the product.

# **6. PHARMACEUTICAL PARTICULARS**

## **6.1 List of excipients**

Povidone Ph.Eur.  
Microcrystalline Cellulose Ph.Eur.  
Colloidal Anhydrous Silica Ph.Eur.  
Sodium Benzoate Ph.Eur.

## **6.2 Incompatibilities**

Not applicable

## **6.3 Shelf-life**

3 years. The dissolved tablet must be taken immediately.

## **6.4 Special precautions for storage**

Do not store above 25°C.

## **6.5 Nature and content of container**

The Pylobactell  $^{13}\text{C}$ -urea breath test kit contains a sachet containing the Pylobactell tablet, six glass tubes with caps and bar code labels, three additional bar code labels, a 30 ml mixing and administration glass vial with cap, two straws, a package leaflet and an Analysis Request Form. A security label for re-sealing the kit is also provided.

The Pylobactell breath test procedure includes the administering of a suitable test meal. This is not supplied within the box.

The Pylobactell tablet container is a heat-sealed PET/aluminium foil/LDPE laminated sachet.

## 6.6 Instructions for use and handling, and disposal

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 is a problem for the patient, then a light breakfast only, e.g. tea and toast, is recommended. If the patient has eaten a heavy meal then it will be necessary to fast for six hours prior to the test.

It is recommended that the breath test is performed while the patient is in a seated position.

### Sampling instructions

t = 0 minutes Note the time the patient drinks the test meal.

t = 5 minutes Collect pre-urea breath samples. Three tubes of breath are to be taken by breathing normally through a straw held at the base of a small tube (white top). The patient must expire as the straw is slowly and completely withdrawn from the tube, which is then immediately capped. These breath samples are used to measure the natural level of  $^{13}\text{C}$  in the carbon dioxide of the breath.

t = 10 minutes The Pylobactell tablet is placed in the 30 ml mixing vial and water added to the marked line. The bottle is capped and shaken well to dissolve the tablet. The entire contents must be swallowed immediately by the patient, the bottle is refilled with water to the line and the entire contents are again swallowed by the patient.

t = 40 minutes Collect post-urea (red top) breath samples. Three tubes of breath are to be taken, which are used to measure the presence of excess levels of  $^{13}\text{C}$ , which will be present if the patient is *H.pylori* positive.

On completion of the test retain one pre-urea sample (white top) and one post-urea sample (red top). Return two pre-urea and two post-urea samples to the box. Safely discard the 30 ml mixing vial. Complete the Analysis Request Form; attach one of three spare bar code labels to the area marked "AFFIX BAR CODE LABEL HERE". This bar code is the doctor's reference number used at the analysing laboratory as a patient identifier; the two spare bar code labels are for the doctor's use on the patient notes/files etc.

After placing the four sample tubes and paperwork into the box, use the security label provided to seal the lid of the box, and send to a qualified laboratory for analysis.

The optimal test meal recommended is 200 ml pure undiluted orange juice.

### Analysis of breath samples and testing specification

Satisfactory specificity and sensitivity have been demonstrated in clinical studies where breath was analysed using isotope ratio mass spectrometry (IRMS). Instrumentation and procedures required for the analysis of breath  $^{13}\text{CO}_2$  enrichment by IRMS are summarised below :

Accuracy and Precision of the test depends heavily on the quality of the breath analysis and thus only laboratories having appropriate certification are qualified to analyse the breath samples.

Breath samples collected during the conduct of a test must be stored in septum capped Exetainer tubes to await enrichment analysis by isotope ratio mass spectrometry (IRMS). Instruments may be of continuous

flow or dual inlet configuration and should preferably be fitted with a multi-position autosampler and bar code reader.

Methodology must be in place to accurately track sample tubes and contents throughout the complete analysis and result reporting stages.

Transfer of the breath sample and the finally purified CO<sub>2</sub> into the mass spectrometer source must be accomplished without incurring isotope fractionation.

The mass spectrometer must possess a triple collector assembly such that ion beams of mass/charge ratio 44, 45 and 46 can be measured simultaneously to allow for correction of the <sup>13</sup>C/<sup>12</sup>C ratio that may result from fluctuations in the oxygen isotope content.

Instrument tuning - Source parameters and major ion beam peak shape must be optimised for each batch of samples.

Instrument stability requires a temperature controlled environment ( $\pm 2^{\circ}\text{C}$ ). Automatic software correction for instrumental drift must be in place. This correction is relative to a reference gas sample introduced every 10 breath samples.

Laboratory reference gas must be standardised against an appropriate international standard to permit interlaboratory comparison of results.

Instrumentation must be linear over a wide range of CO<sub>2</sub> concentrations (typically 0.5 - 5.0%; total ion current  $5 \times 10^{-8}$  -  $8 \times 10^{-7}$  A respectively ) and this must be routinely checked.

Internal analytical precision must be less than  $\pm 0.2\%$   $\delta^{13}\text{C}$  for 30 replicate analyses of the same reference gas sample and remain within 2SD's of the mean for breath analyses.

Explanation of results :-

$\delta^{13}\text{C}$  :- Difference in parts per thousand (‰) with respect to an accepted international standard

Excess  $\delta^{13}\text{C}$  :- Difference between pre- and post-urea sample measurements

*H. pylori* status :-  $< 3.5$  excess  $\delta^{13}\text{C}$  = Negative  
 $\geq 3.5$  excess  $\delta^{13}\text{C}$  = Positive

Alternatively, any other suitably-validated method may be used, carried out by any objectively qualified laboratory.

## **7. MARKETING AUTHORISATION HOLDER**

Torbet Laboratories Limited  
14D Wendover Road  
Rackheath Industrial Estate  
Norwich  
Norfolk  
NR13 6LH  
United Kingdom

## **8. MARKETING AUTHORISATION NUMBER**

EU/1/98/064/001

**9. DATE OF FIRST AUTHORISATION**

7 May 1998

**10. DATE OF REVISION OF THE TEXT/ RENEWAL OF THE AUTHORISATION**

**ANNEX II**

- A. MANUFACTURING AUTHORISATION HOLDER  
RESPONSIBLE FOR BATCH RELEASE**
  
- B. CONDITIONS OF THE MARKETING AUTHORISATION**

**A. MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer responsible for batch release

PackPharm Limited  
14D Wendover Road  
Rackheath Industrial Estate  
Norwich  
Norfolk  
NR13 6LH  
United Kingdom

**B. CONDITIONS OF THE MARKETING AUTHORISATION**

• **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription

• **OTHER CONDITIONS**

The holder of this marketing authorisation must inform the European Commission about the marketing plans for the medicinal product authorised by this decision.

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING OR, WHERE THERE IS NO OUTER PACKAGING, ON THE IMMEDIATE PACKAGING**

**{OUTER CARTON/CARDBOARD BOX}**

**1. NAME OF THE MEDICINAL PRODUCT**

Pylobactell  
100 mg  
soluble tablet  
<sup>13</sup>C-urea

**2. STATEMENT OF ACTIVE SUBSTANCES**

The tablet contains: <sup>13</sup>C-urea 100 mg

**3. LIST OF EXCIPIENTS**

Povidone, Microcrystalline Cellulose (E460), Colloidal Anhydrous Silica, Sodium Benzoate (E211).

**4. PHARMACEUTICAL FORM AND CONTENTS**

The kit contains:

A sachet containing one Pylobactell 100 mg tablet.  
Six glass tubes, with caps and bar code labels.  
30 ml mixing and administration glass vial with cap.  
Two straws.  
Package Leaflet.  
Analysis Request Form.  
Security Label and three additional bar code labels.

**5. METHOD AND ROUTE OF ADMINISTRATION**

Diagnostic test kit  
FOR SINGLE USE  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF REACH AND SIGHT OF CHILDREN**

Keep out of the reach and sight of children.

**8. EXPIRY DATE**

EXP : {MM/YYYY}

**9. SPECIAL STORAGE CONDITIONS**

Do not store above 25°C

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Torbet Laboratories Ltd, Norwich, Norfolk, NR13 6LH, United Kingdom.

**12. MARKETING AUTHORISATION NUMBER**

EU/1/98/064/001

**13. MANUFACTURERS BATCH NUMBER**

Batch

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

{SACHET LABEL}

**1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION**

Pylobactell  
100 mg  
soluble tablet  
<sup>13</sup>C-urea

**2. METHOD OF ADMINISTRATION**

To be dissolved in water and taken orally

**3. EXPIRY DATE**

EXP {MM/YYYY}

**4. BATCH NUMBER**

Batch

**5. NAME AND ADDRESS OF MARKETING AUTHORISATION HOLDER**

Torbet Laboratories Limited, Unit 14D, Wendover Road, Rackheath Industrial Estate, Norwich,  
Norfolk, NR13 6LH, United Kingdom.

**6. MARKETING AUTHORISATION NUMBER**

EU/1/98/064/001

**ADDITIONAL KIT ITEM: MIXING AND ADMINISTRATION VIAL**

**{LABEL}**

Fill to line with water  
Dissolve tablet from sachet  
Shake well to dissolve  
When dissolved, drink entire contents  
Refill with water to line, shake bottle and drink  
Discard this bottle after use  
Do not return with kit

**ADDITIONAL KIT ITEM: SECURITY LABEL**

**{LABEL}**

Seal lid of box before returning samples for analysis

**B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

Please read all of this leaflet carefully before you start taking the Pylobactell Breath Test.  
If you have any questions or are not sure about anything, please ask your doctor.  
Keep this leaflet, you may need to read it again.  
This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same.

### **PYLOBACTELL.100 mg. Soluble tablet**

<sup>13</sup>C-urea

### **WHAT DOES THE PYLOBACTELL BREATH TEST CONTAIN?**

Each Pylobactell Breath Test kit contains:

Sachet containing one tablet.

The tablet contains 100 mg of the active ingredient <sup>13</sup>Carbon (<sup>13</sup>C) urea. The other ingredients are Povidone, Microcrystalline Cellulose (E460), Colloidal Anhydrous Silica and Sodium Benzoate (E211) to form the tablet.

The kit also contains:

Six glass tubes, with caps and bar code labels.

30 ml mixing and administration glass vial with cap.

Two straws.

Package Leaflet (this leaflet).

Analysis Request Form.

Security Label and three additional bar code labels.

The contents of this kit are sufficient for a single test. If you need to repeat the test, it should not be carried out until the following day.

The Pylobactell Breath Test is a test for determining the presence of *Helicobacter pylori* in the gut (stomach and adjacent bowel).

The reliability of the Pylobactell breath test has not been proven in patients who have had part of their stomach removed (partial gastrectomy); in patients with documented or suspected gastric infection; in cases of atrophic gastritis and under 18 years.

### **Marketing Authorisation Holder:**

Torbet Laboratories Limited, 14D Wendover Road, Rackheath Industrial Estate, Norwich, Norfolk, NR13 6LH, United Kingdom.

### **Manufacturer**

PackPharm Limited, 14D Wendover Road, Rackheath Industrial Estate, Norwich, Norfolk, NR13 6LH, United Kingdom.

### **WHY DO YOU NEED TO TAKE THE PYLOBACTELL BREATH TEST?**

It is possible that your gastric condition is associated with infection by a bacterium called *Helicobacter pylori*. Your doctor has recommended that you have a <sup>13</sup>C-Urea Breath Test, which is a simple test for determining the presence of active *Helicobacter pylori* in the gut, for one of the following reasons:-

- Your doctor wants to confirm whether you are suffering from *Helicobacter pylori* infection to help diagnose your condition.

- You have already been diagnosed as being infected with *Helicobacter pylori* and have been taking medication aimed to clear up the infection. Your doctor now wishes to find out if the treatment has been successful.

This medicinal product is for diagnostic use only.

### **How does the test work?**

All foods contain a substance called <sup>13</sup>carbon (“carbon 13” <sup>13</sup>C), in varying amounts. This <sup>13</sup>carbon can be detected in the carbon dioxide that you breathe out of your lungs. The actual amount of <sup>13</sup>carbon in the breath will depend on the type of food that you have eaten.

You will be asked to drink the "test meal". This will help keep the test solution in your stomach.

Following the meal, three samples of your breath will be taken. These samples will be analysed to measure the normal amount of <sup>13</sup>carbon in the carbon dioxide in your breath.

You will then drink the test solution of <sup>13</sup>carbon-urea (urea made from <sup>13</sup>carbon). If active *Helicobacter pylori* are present in your stomach, these bacteria will break down the <sup>13</sup>carbon-urea, releasing <sup>13</sup>carbon into the carbon dioxide in your breath.

Further samples of your breath will then be taken 30 minutes later.

The amount of <sup>13</sup>carbon in these samples will be compared to your normal level and a significant increase in the amount of <sup>13</sup>carbon in the second set of samples will suggest to your doctor that active *Helicobacter pylori* are present.

### **BEFORE TAKING THE TEST**

**Do not take Pylobactell** if you are hypersensitive (allergic) to <sup>13</sup>Carbon (<sup>13</sup>C) urea or to any of the other ingredients used to form the tablets: Povidone, Microcrystalline Cellulose (E460), Colloidal Anhydrous Silica and Sodium Benzoate (E211).

Please tell your doctor if you suffer from any medical condition that you think may affect, or be affected by, the test. It is also important that you tell your doctor if any of the following circumstances apply to you:

#### Other Medication:

For pre-treatment testing, the test should not be carried out if you are currently taking, or have taken in the last 14 days, certain medication.

Show or tell your doctor what you have been taking.

For post-treatment testing, if your doctor has prescribed medication for killing the bacteria it is essential that the test is not used within 28 days of completing treatment.

#### **Fasting:**

You will need to fast so that the test is taken on an empty stomach.

If fasting is a problem e.g. for diabetic patients, please tell your doctor.

You should fast for at least 4 hours before the test.

If the test is to be carried out in the morning you will be asked to fast overnight and not to eat breakfast. If the test is to be carried out later in the day, or if a long fast is a problem for you, a light breakfast e.g. tea and toast is recommended.

If you have eaten a heavy meal it will be necessary to fast for six hours before the test.

You can drink water during the fasting period.

Additional items not included with the Pylobactell Breath Test:

You will need some drinking water to carry out the test.

An important part of the Pylobactell Breath Test is the drinking of a liquid test meal to delay the emptying of your stomach.

THIS IS NOT INCLUDED IN THIS KIT but may have been supplied separately.

The most suitable test meal is 200 ml of pure undiluted orange juice.

If you suffer from a food allergy or there are certain food groups that you have been recommended to avoid for medical reasons, please tell your doctor. Your doctor will wish to ensure that the test meal is suitable for you to take.

An alternative test meal will be provided if you are unable to take the one initially offered to you.

**PREGNANCY AND BREAST-FEEDING**

Pylobactell can be used during pregnancy and breast-feeding.

**Driving and using machines**

This test should not affect your ability to drive or use machines.

**THE TEST PROCEDURE**

It is recommended that the breath test is performed while you are in a seated position.

You should not smoke immediately before or during the test.

You should not eat or drink during the test.

The test procedure involves the following steps:

(A brief form of these instructions is included on the back of the Analysis Request Form)

1. Fasting: (See 'Before taking the test')
2. Test Meal: Drink the recommended test meal (see 'Before taking the test').
3. Wait 5 minutes
4. Breath Samples ("Pre" White Caps)  
Using each of the white-capped, white-labelled tubes take a sample of your breath.
  - i. Remove the cap from the tube
  - ii. Breathe out through your mouth, using a straw, into the sample tube.
  - iii. Gradually remove the straw from the tube as you breathe out.
  - iv. Immediately replace the cap.

It is not necessary to blow hard into the tubes, just breathe normally and cap them quickly.

Tubes with saliva in them cannot be analysed.

5. <sup>13</sup>Carbon-urea solution  
Open the tablet sachet and empty the tablet into the mixer vial.  
Add water to the mark on the vial and replace the cap.  
Gently shake the vial to dissolve the tablet.  
Drink the solution. Note the time upon drinking.  
Fill the vial to the mark again with water and drink.

6. Wait 30 minutes from the time of drinking the solution. This is important for the proper functioning of the test.
7. Breath Samples (“Post” Red Caps)  
Using the red-capped, red-labelled tubes, take samples of your breath as before (see step 4).
8. Finish Up  
The test is now complete.  
Put your breath samples and the completed Analysis Request Form back into the carton  
Send to a qualified laboratory for analysis as directed by your doctor.

The empty sachet, mixing vial and straws can be disposed of as normal waste.

You should keep this leaflet for reference.

Your doctor will tell you when the results of your test will be available and who to contact for these results.

#### **Will you experience any side effects after the test?**

<sup>13</sup>Carbon is a harmless naturally occurring substance which is found in the body. Urea is also a harmless substance which is found in the body.

No side effects to Pylobactell have been reported. If you notice any side effects, please inform your doctor or pharmacist.

#### **EXPIRY DATE**

The test kit carton is marked with an expiry date.  
The kit should not be used after this date.

#### **Storage**

Keep out of the reach and sight of children.

The kit should not be stored above 25°C.  
The dissolved tablet must be taken immediately.

Do not use after the expiry date stated on the carton.

#### **Further Information:**

For any information about this medicinal product, please contact the Marketing Authorisation Holder.

Torbet Laboratories Limited, 14D Wendover Road, Rackheath Industrial Estate, Norwich, Norfolk, NR13 6LH, United Kingdom.

Tel : (+44) 1603 735200

**This leaflet was last approved on**

### Analysis of breath samples and testing specification

Satisfactory specificity and sensitivity have been demonstrated in clinical studies where breath was analysed using isotope ratio mass spectrometry (IRMS). Instrumentation and procedures required for the analysis of breath  $^{13}\text{CO}_2$  enrichment by IRMS are summarised below :

Accuracy and Precision of the test depends heavily on the quality of the breath analysis and thus only laboratories having appropriate certification are qualified to analyse the breath samples.

Breath samples collected during the conduct of a test must be stored in septum capped Exetainer tubes to await enrichment analysis by isotope ratio mass spectrometry (IRMS). Instruments may be of continuous flow or dual inlet configuration and should preferably be fitted with a multi-position autosampler and bar code reader.

Methodology must be in place to accurately track sample tubes and contents throughout the complete analysis and result reporting stages.

Transfer of the breath sample and the finally purified  $\text{CO}_2$  into the mass spectrometer source must be accomplished without incurring isotope fractionation.

The mass spectrometer must possess a triple collector assembly such that ion beams of mass/charge ratio 44, 45 and 46 can be measured simultaneously to allow for correction of the  $^{13}\text{C}/^{12}\text{C}$  ratio that may result from fluctuations in the oxygen isotope content.

Instrument tuning - Source parameters and major ion beam peak shape must be optimised for each batch of samples.

Instrument stability requires a temperature controlled environment ( $\pm 2^\circ\text{C}$ ). Automatic software correction for instrumental drift must be in place. This correction is relative to a reference gas sample introduced every 10 breath samples.

Laboratory reference gas must be standardised against an appropriate international standard to permit interlaboratory comparison of results.

Instrumentation must be linear over a wide range of  $\text{CO}_2$  concentrations (typically 0.5 - 5.0%; total ion current  $5 \times 10^{-8}$  -  $8 \times 10^{-7}$  A respectively ) and this must be routinely checked.

Internal analytical precision must be less than  $\pm 0.2 \text{‰ } \delta^{13}\text{C}$  for 30 replicate analyses of the same reference gas sample and remain within 2SD's of the mean for breath analyses.

#### Explanation of results :-

$\delta^{13}\text{C}$  :- Difference in parts per thousand ( ‰ ) with respect to an accepted international standard

Excess  $\delta^{13}\text{C}$  :- Difference between pre- and post-urea sample measurements

H. pylori status :-  $< 3.5$  excess  $\delta^{13}\text{C}$  = Negative  
 $\geq 3.5$  excess  $\delta^{13}\text{C}$  = Positive

Alternatively, any other suitably-validated method may be used, carried out by any objectively qualified laboratory.

**ANALYSIS REQUEST FORM:**

Pylobactell [<sup>13</sup>Carbon] -UREA BREATH TEST (<sup>13</sup>C-UBT) for Helicobacter pylori

ANALYSIS REQUEST FORM - Please complete in block capitals

Please state clearly address for return of results:

Centre:  
Patient Name:  
Date of Birth:  
Patient Reference:  
Date of Test:  
Referring Doctor:

AFFIX BAR-CODE LABEL HERE

PLEASE PLACE BAR-CODE LABEL ON PATIENT RECORDS, IF APPLICABLE

M.A. Number:  
Marketing Authorisation Holder: EU/1/98/064/001  
Torbet Laboratories Limited, Norwich, Norfolk, NR13 6LH, United Kingdom

MEDICATION RECORD	Type & Date	Mins	TEST CHECK LIST	Time
<u>Medical History</u> - has the patient taken :			Test Check List	
<u>(i) antibiotics in the last 28 days?</u> If so, please indicate type and when last taken		<u>t = 0</u>	Note time patient drinks test meal	
<u>(ii) proton pump inhibitors (PPIs) in the last 14 days?</u> If so, please indicate type and when last taken.		<u>t = 5</u>	Collect Pre-Urea samples (White Caps - 3 times)	
<u>(iii) eradication therapy in the last 28 days?</u> If so, please indicate when treatment ended		<u>t = 10</u>	Patient to drink urea solution, then fill bottle to line again and drink.	
<u>(iv) other medication (if applicable)</u>		<u>t = 40</u>	Collect Post-Urea samples (Red Caps - 3 times).	
<u>(v) patient fasted for hours</u>		<u>Check</u>	Bar-code label and all details entered on Analysis Request Form. 1 x Pre/Post sample reserved in store. 2 x Pre/Post samples + this form for return to a qualified laboratory.	
Please note that (i) - (iii) will affect result of test.				
<u>Laboratory use only</u> Date received: Analytical file reference: Laboratory code: Samples logged on by :			Comments:	

