13C-urea breath testing for *Helicobacter pylori*. 
Urea breath testing

What is the PYLOBACTELL 13C-Urea Breath test and how does it work?

The 13C-Urea Breath Test (13C-UBT) is recognised by Healthcare Professionals [1], [2] as the easiest, safest and most reliable non-invasive test for identifying Helicobacter pylori status. It is essential to remember that 13C is a stable isotope and therefore has no associated radioactivity. It should not be confused with the 14C radioactive isotope.

The 13C-UBT takes full advantage of the strong urease activity of H pylori. Effectively if urea is introduced into the gut, the H. pylori urease enzyme will hydrolyse the urea into ammonia and carbon dioxide. The carbon dioxide produced will be absorbed into the blood system, transported to the lungs and exhaled. If the urea is labelled with the non-radioactive isotope 13C and introduced into the gut colonised by H. pylori, the CO₂ produced will be labelled with 13C. If H. pylori is not present the urea will pass through the gut with no immediate change in the 13C content of the exhaled CO₂.

Our exhaled breath naturally contains 13C (1.1% of normal body Carbon is 13C). It is therefore necessary to measure a patient’s basal 13CO₂ content (Pre-Dose sample) before drinking the 13C-Urea solution. Peak excretion of 13CO₂ in H. pylori positive subjects is thirty minutes after drinking the 13C-Urea solution (Post-Dose sample).

The difference in 13C content between the Post-Dose and the Pre-Dose samples is expressed as “excess 13C”. It is the excess value which is recorded on reports to distinguish between H. pylori negative or positive. Excess 13C values greater than 3.5 per mil indicate an H. pylori positive status.

In the UK, the 13C UBT was extensively tested in the late 1980’s against recognised biopsy methods by the Central Middlesex group under Dr George Misiewicz. These comparisons have been well documented in two publications:

Safety of the Test

The 13C urea breath test is a development of the 14C urea breath test. Where the radioactive nature of 14C means the test is limited to facilities able to handle the compound, 13C-urea tests can be performed by patients and clinical staff. Although the analysis requires instruments not normally found in primary or secondary care, analysis is routinely handled by external laboratories able to cater for the whole healthcare sector regardless of customer size or frequency of testing need.

The 13C-UBT is completely safe and is regularly used in paediatric studies and is safe for use by expectant mothers. 13C is naturally occurring and represents 1.1% of all Carbon in our body. Therefore, in an average 70kg adult there are 192 grams of 13C naturally present. The normal daily food intake of a 70kg adult will contain approximately 3 grams of 13C.

During the Pylobactell 13C-UBT the subject takes 100 mg 13C-Urea which only represents a further 0.7% of 13C on top of their normal daily intake of 13C. The amount of Urea (100mg) which the subject takes during the breath test is only a small percentage of the average total body urea pool of 10g.
Breath Testing Information Sheet: Medication

Torbet Laboratories Ltd recommend that certain medication which may influence the $^{13}$C-UBT and could give a false negative result should be avoided prior to the test.

The classes of medication and abstention period are as follows:

<table>
<thead>
<tr>
<th>Class Of Medication</th>
<th>Examples of Medication</th>
<th>Abstention period</th>
</tr>
</thead>
<tbody>
<tr>
<td>$H. pylori$ eradication therapy</td>
<td>HeliMet “triple therapy”</td>
<td>28 days before test</td>
</tr>
<tr>
<td>Oral Antibiotics</td>
<td>Amoxycillin</td>
<td>28 days before test</td>
</tr>
<tr>
<td>Bismuth compounds</td>
<td>DeNol, bismuth subcitrate</td>
<td>28 days before test</td>
</tr>
<tr>
<td>Proton Pump Inhibitors (PPI’s)</td>
<td>Omeprazole, Lanzoprazole, Zoton</td>
<td>14 days before test</td>
</tr>
<tr>
<td>H2 Receptor Antagonists</td>
<td>Zantac, Cimetidine, Ranitidine</td>
<td>12 hours before the test</td>
</tr>
<tr>
<td>Antacid preparations</td>
<td>Gaviscon</td>
<td>12 hours before the test</td>
</tr>
</tbody>
</table>

There are a few natural remedies promoted for treating ulcers and/or by inference $H. pylori$. If the patient is taking any medication or natural remedies with the specific intention of treating an $H. pylori$ infection this should be noted.

If you have any queries about particular medication, please contact us and we will advise as to compatibility with Pylobactell.

If you have any queries about the information on this sheet or any other issue about Pylobactell, please contact us.

**Pylobactell Support Line 01953 607856**
Breath Testing Information Sheet: **Test Meal**

The test meal is part of the testing procedure. It delays gastric emptying, allowing increased retention time of the urea solution within the stomach.

Most patients are able to use the supplied test meal. However if this is unsuitable for the patient, an alternative can be used:

**Suitable test meals for Pylobactell \( ^{13} \text{C-UBT} \)**

<table>
<thead>
<tr>
<th>Citrace sachet(^1) (lemon flavoured ascorbic acid)</th>
<th>As supplied with Pylobactell test. Dissolve contents of sachet in 200ml of drinking water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>200ml of full cream milk. Especially if the patient has difficulty with high acidity drinks</td>
</tr>
<tr>
<td>Orange Juice(^2)</td>
<td>200ml of pure orange juice</td>
</tr>
<tr>
<td>Bread and butter</td>
<td>Two slices of brown bread, buttered. (Margarine and other vegetable spreads are not recommended)</td>
</tr>
</tbody>
</table>

**Notes**

1. Citrace contains a source of phenylalanine. May be harmful for people with phenylketonuria.

2. Orange squash and diluted orange juice are not suitable substitutes for the Citrace sachet or orange juice.

If none of the Test Meals listed above is suitable for the patient, please contact Torbet Laboratories.

If you have any queries about the information on this sheet or any other issue about Pylobactell, please contact us.

**Pylobactell Support Line** 01953 607856
Breath Testing Information Sheet: The Diabetic Patient

Since the Pylobactell breath test requires a fasting period, there may be some concerns about the suitability for use in diabetic patients. Each patient for whom fasting may be an issue should be considered individually so this information sheet gives pertinent background information to help the clinician make a judgement.

Test timing and food intake
The test is performed after a 4 hour fast (6 hours after a large meal). The test starts with a test meal* (an ascorbic acid solution or pure fruit juice) The test then takes approx 40 minutes to complete.

* Test meal is covered by Pylobactell Information sheet No 2

Patient Constraints
The patient can

- Eat or drink immediately the test is completed
- Perform the test at home to fit their routine rather than conform to surgery hours/appointment
- Take water during the fasting period

Patient Medication (insulin use)

Unless medication is known to affect:
- Stomach emptying rate
- Acid production within the stomach
- Activity of H. pylori urease
- CO₂ elimination through the lungs
- Deliver carbonate with unusual levels of 13C into gut or blood

We presume there is no effect on test performance, and we believe none of the above apply to insulin injections or oral insulin

If you have any queries about the information on this sheet or any other issue about Pylobactell, please contact us.

Pylobactell Support Line 01953 607856
Breath Testing Information Sheet: Composition

This sheet gives information on the composition of the Pylobactell tablet and Torbet Laboratories 'Test Meal'.

Pylobactell Tablet - $^{13}$C -urea soluble tablet

Active ingredient
$^{13}$C Urea 100mg

Excipients 15 mg total
  Povidone
  Sodium benzoate
  Microcrystalline cellulose
  Colloidal anhydrous silica

To be dissolved in 30ml of water during the test procedure

Test Meal - Citrace

The test meal provided by Torbet Laboratories for use with Pylobactell is a lemon-flavoured sweetened ascorbic acid mixture. ¹

Citrace is supplied as a foiled sachet containing 1g of powder to be made up to 200ml with water. Each sachet contains:

Ascorbic acid (E300)
Lemon flavour
Aspartame (E591)*
*Aspartame is a source of phenylalanine. May be harmful to people with phenylketonuria.

Each test meal carries an expiry date crimped on the side of the sachet.

1) Alternative test meals are covered by Information Sheet No. 2

Pylobactell Support Line 01953 607856

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Torbet Laboratories Ltd
Units 1&2 Chestnut Drive, Wymondham, Norfolk, NR18 9SB
Tel 01953 607856 Fax 01953 713649
email:pylobactell@breathlab.com

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Breath Testing Information Sheet: Analysis

This sheet gives information on the analysis of the samples from the Pylobactell breath test kit by Torbet Laboratories Ltd.

Analysis of Pylobactell samples by Torbet Laboratories is covered by our Quality System which is accredited by UKAS against an international standard.

UKAS
UKAS, the United Kingdom Accreditation Service, is the only body recognised by the government to assess the ability of laboratories against international standards. For Torbet Laboratories the standard is ISO 17025:2005.

Assessment
UKAS uses its own assessors to determine if a laboratory is able to meet the standard; once accepted the laboratory is subject to yearly assessments. All aspects of the work and the management of the laboratory are described in written procedures and considered by the assessors during evaluation and assessment.

Accreditation
Accreditation by UKAS demonstrates the competence, impartiality and performance capability of our laboratory so you can be "...sure that the laboratory has the people, facilities, technical expertise, management systems and track record to do the job right. Each time, every time."

ISO 9000
Some laboratories may have the ISO 9000 standard, however this only relates to management systems used, it does not specifically evaluate the technical competence. The management system requirements of ISO 17025:2005 (the latest standard) meet the principles of ISO 9001:2000.

Accreditation mark
Test reports issued under our management system carry our UKAS registration mark and number.

Don't risk it. UKAS brochure (2005)
Joint ISO-ILAC-IAF communiqué (18/06/2005), www.ukas.com

Pylobactell Support Line 01953 607856

Torbet Laboratories Ltd
Units 1&2 Chestnut Drive, Wymondham, Norfolk, NR18 9SB
Tel 01953 607856  Fax 01953 713649
email:pylobactell@breathlab.com
CONFIRM PATIENT FASTED AND OFF MEDICATION
PUT PATIENT DETAILS ON ‘ANALYSIS REQUEST FORM’

PATIENT DRINKS TEST MEAL

10:00

PATIENT GIVES PRE-UREA BREATH SAMPLES
3 X WHITE CAPS WHITE LABELS

PREPARE UREA SOLUTION

10:05

PATIENT DRINKS UREA SOLUTION

10:10

PATIENT WAITS 30 MIN
SEATED
NO FOOD OR DRINK
NO SMOKING

PATIENT GIVES POST-UREA BREATH SAMPLES
3 X RED CAPS RED LABELS

10:40

REPACK TUBES WITH ANALYSIS REQUEST FORM AND SEAL
SEND OFF IN FREEPOST ENVELOPE
DISCARD VIAL, STRAWS AND SACHET

DONE

See the Pylobactell Information Sheet 1 for Medication Data

Alternative Test Meals can be used
See Information Sheet 2

Don’t cover Barcodes with Patient Labels
BLOW GENTLY
No Saliva

Drink, Refill with Water and Drink Again

Keep Pair of Tubes if required
Use Extra Barcode Labels on Patient Records as Necessary

Supplied as a service by Torbet Laboratories Limited, manufacturer of the Pylobactell $^{13}$C Urea Breath Test kit and provider of Laboratory Services for the analysis of $^{13}$C in breath samples.

For all Pylobactell Enquiries
Tel: 01953 607856
Fax: 01953 713649
Email: Pylobactell@breathlab.com

Torbet Laboratories Ltd
FREEPOST RSSX-TSLG-XSET
Chestnut Drive
Wymondham
NR18 9SB
IMPORTANT - BEFORE YOUR TEST

You will have been given instructions about preparation for the test. These are repeated here. If you have been given instructions that are different to these, then you should follow the advice of your doctor.

For the best result from your test it is important that:

You take the test on an empty stomach.

Please do not eat or drink (except water) for at least 4 hours before the test. If fasting is a problem, please ask the advice of your doctor.

You should not have taken certain medicines in the time before the test:

Antibiotics
   (e.g. penicillin, metronidazole)
   - 28 days before the test
Proton Pump Inhibitors
   (e.g. lansoprazole, omeprazole)
   - 14 days before the test
H2 antagonists, antacids
   (e.g. ranitidine, cimetidine, Gaviscon)
   - 12 hours before the test
Do not stop taking any medicine unless told to by your doctor.

You may be asked about medicines you are taking when you take the test. If you are unsure about the name or type of your medicine, bring it, the packet, or the patient information leaflet along with you.

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**THE $^{13}$C-UREA BREATH TEST**

**WHAT IS *HELCOBACTER PYLORI*?**

This is a bacterium that lives in lining of the stomach and gut. It may be a life-long infection that generally causes no problems. However, it is often associated with dyspepsia (indigestion) and peptic (stomach) ulcer. Treatment of the bacteria with medication can allow the ulcer to heal.

**WHAT DOES THIS TEST DO?**

Helicobacter pylori breaks down urea, a common substance in many foods, into ammonia and carbon dioxide. Your test is based on this unique feature of the bacteria.

Urea that is high in a substance known as Carbon-13 ("$^{13}$C") is used ($^{13}$C-urea). $^{13}$C can be measured by laboratory equipment. If the bacteria are present this $^{13}$C will appear in the carbon dioxide in your breath. Examination of samples of your breath taken before and after consuming the $^{13}$C-urea will show if the bacteria are present in your stomach.

**WHAT IS IN THE TEST?**

Urea is a harmless substance found in food and in your body. $^{13}$C is a harmless naturally occurring substance that is present all around us. It is not radioactive.

The amounts of these substances that you take during the test are very small compared to the amounts already present in your body or that you eat in your normal diet.

If you have any food allergies or intolerances you should speak to your doctor or other health professional before taking the test.

**WHAT WILL HAPPEN IN THE TEST?**

The test requires you to drink a "test meal" which will be a glass of lemon-flavoured drink, or orange juice. If you are allergic to either of these or have difficulty drinking acidic drinks, please contact the test centre to arrange an alternative.

You will give samples of your breath by blowing into a set of tubes.

You will drink a small quantity of $^{13}$C-Urea dissolved in water (60ml). This is a colourless and tasteless liquid.

You will then be asked to sit quietly, without eating, drinking, or smoking for 30 minutes.

Finally, you will give more samples of your breath to complete the test.

**WHEN WILL I KNOW THE RESULT?**

The samples of breath have to be sent away to be analysed at a laboratory. You will be given a date to contact your doctor to learn the results of the test.

**IS THERE ANYTHING I HAVE TO DO?**

You will have to fast (not eat) before you take the test.

Some medications that you might take can affect the accuracy of the test.

Please read the **Important Information** overleaf.

**PYLOBACTELL UREA BREATH TEST PROCEDURE**

- Drink "Test Meal" & Wait 5 minutes
- Blow into Pre-Test (white cap) Tubes
- Drink Urea Solution & Wait 30 minutes
- Blow into Post-Test (red cap) Tubes
- Test Completed
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Pylobactell 100 mg soluble tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soluble tablet contains 100 mg of $^{13}$C-urea

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Soluble tablet.
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 (H. 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.

The patient should fast for at least 4 hours before the test so that the test is taken on an empty stomach. If the patient has eaten a heavy meal, then it will be necessary to fast for 6 hours prior to the test.

*Paediatric patients:* Pylobactell is not recommended for use in children and adolescents below the age of 18 years due to insufficient data on efficacy.

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 Contraindications

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

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

4.4 Special warnings and 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, e.g. 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 (see section 4.2).

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 medicinal products. 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 breast-feeding.

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 breast-feeding.

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: V04CX.
In the case of infection with *H. pylori*, orally ingested $^{13}$C-urea is metabolised by the enzyme urease which is present in *H. pylori*.

$$\text{H}_2\text{N}(^{13}\text{CO})\text{NH}_2 + \text{H}_2\text{O} \rightarrow 2\text{NH}_3 + ^{13}\text{CO}_2$$

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 $^{13}$CO$_2$ in exhaled air. Infection with *H. pylori* will significantly change the $^{13}$C/$^{12}$C - carbon isotope ratio.

The proportion of $^{13}$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 (pre-study 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 (E1201)
Microcrystalline cellulose (E460i)
Colloidal anhydrous silica
Sodium benzoate (E211)

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 contents of container

The Pylobactell $^{13}$C-urea breath test kit contains a heat-sealed PET/aluminium foil/LDPE laminated sachet containing one 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.

6.6 Special precautions for disposal and other handling

The patient should fast for at least 4 hours before the test so that the test is taken on an empty stomach. If the patient has eaten a heavy meal then it will be necessary to fast for 6 hours prior to the test.

It is recommended that the breath test is performed while the patient is in a seated position. The Pylobactell breath test procedure includes the administering of a suitable test meal. This is not supplied within the box. The optimal test meal recommended is 200 ml pure undiluted orange juice.

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 $^{13}$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 $^{13}$C, which will be present if the patient is $H.\text{pylori}$ 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.

Analysis of breath samples and testing specification

The accuracy and precision of the test depends heavily on the quality of the analysis and therefore only laboratories having appropriate certification are considered qualified to analyse the breath samples.
Satisfactory specificity and sensitivity have been demonstrated in clinical studies where breath was analysed using isotope ratio mass spectrometry (IRMS).

Breath samples collected during the test must remain in the original containers before analysis by IRMS.

IRMS instruments may be of continuous flow or dual inlet configuration.

A multi-position auto-sampler and bar code reader should be used to allow samples to be tracked throughout the analysis.

IRMS source parameters and tuning must be optimised daily.

Instruments must be linear over a wide range of CO₂ concentrations typically 1.0 - 6.0%. This should be checked routinely.

Internal analytical precision must be less than \( \pm 0.3 \ \% \delta^{13}C \) for 20 replicate analyses of the same reference gas sample and remain within \( 3\sigma \)’s of the mean for breath analyses.

Transfer of the breath sample through the analytical system must be accomplished without isotope fractionation.

The IRMS must possess a triple collector to allow the simultaneous detection of the ions at mass/charge ratio 44, 45 and 46 fluctuations in the oxygen isotope content.

There must be provision for correction of instrumental drift during an analysis.

Reference gases must be standardised against an appropriate international standard to allow inter-laboratory comparison of results.

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

**Explanation of results:**

\( \delta^{13}C \):- Difference in parts per thousand (‰) with respect to an accepted international standard.
Excess \( \delta^{13}C \):- Difference between pre- and post-urea sample measurements.

\( H. \text{ pylori} \) status: 

\(< 3.5 \ \text{excess } \delta^{13}C = \text{Negative} \)

\( \geq 3.5 \ \text{excess } \delta^{13}C = \text{Positive} \)

7. MARKETING AUTHORISATION HOLDER

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

\(+44 (0)1603 \ 735200\)
8. MARKETING AUTHORISATION NUMBER

EU/1/98/064/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 7 May 1998
Date of latest renewal: 7 May 2008

10. DATE OF REVISION OF THE TEXT

05/2008

Detailed information on this medicinal product is available on the website of the European Medicines Agency (EMEA) http://www.emea.europa.eu/.
United Kingdom Accreditation Service

ACCREDITATION CERTIFICATE

TESTING LABORATORY
No. 2556

Torbet Laboratories Limited

is accredited in accordance with the recognised International Standard ISO/IEC 17025:2005 General Requirements for the competence of testing and calibration laboratories.

This accreditation demonstrates technical competence for a defined scope as detailed in and at the locations specified in the schedule to this certificate, and the operation of a laboratory quality management system (refer joint ISO-ILAC-IAF Communiqué dated January 2009).

The schedule to this certificate is an essential accreditation document and from time to time may be revised and reissued by the United Kingdom Accreditation Service. The most recent issue of the schedule of accreditation, which bears the same accreditation number as this certificate, is available from the UKAS website www.ukas.com.

This accreditation is subject to continuing conformity with United Kingdom Accreditation Service requirements. The absence of a schedule on the UKAS website indicates that the accreditation is no longer in force.

Accreditation Manager, United Kingdom Accreditation Service

Initial Accreditation date
28 May 2004

This certificate issued on
21 August 2012

UKAS is appointed as the sole national accreditation body for the UK by The Accreditation Regulations 2009 (SI No 3155/2009) and operates under a Memorandum of Understanding (MoU) with the Department for Business, Innovation and Skills (BIS).
# Schedule of Accreditation

**Issued by**

**United Kingdom Accreditation Service**

21 - 47 High Street, Feltham, Middlesex, TW13 4UN, UK

---

**Torbet Laboratories Limited**

**Issue No:** 007  **Issue date:** 19 December 2012

<table>
<thead>
<tr>
<th>Units 1-2</th>
<th>Contact: Mr Graeme Leggett</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wymondham Business Park</td>
<td>Tel: +44 (0)1953 607856</td>
</tr>
<tr>
<td>Chestnut Drive</td>
<td>Fax: +44 (0)1953 713649</td>
</tr>
<tr>
<td>Wymondham</td>
<td>E-Mail: <a href="mailto:GraemeLeggett@breathlab.com">GraemeLeggett@breathlab.com</a></td>
</tr>
<tr>
<td>Norfolk</td>
<td>Website:</td>
</tr>
<tr>
<td>NR18 9SB</td>
<td></td>
</tr>
</tbody>
</table>

**Testing performed at the above address only**

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## DETAIL OF ACCREDITATION

<table>
<thead>
<tr>
<th>Materials/Products tested</th>
<th>Type of test/Properties measured/Range of measurement</th>
<th>Standard specifications/Equipment/Techniques used</th>
</tr>
</thead>
<tbody>
<tr>
<td>HUMAN BREATH SAMPLES</td>
<td>Chemical Tests</td>
<td>Documented In-House Methods using Gas Chromatography and Stable Isotope Ratio Mass Spectrometry</td>
</tr>
<tr>
<td></td>
<td>Determination and comparison of the $^{13}\text{C}/^{12}\text{C}$ ratios in carbon dioxide from exhaled breath collected as part of a 100 mg $^{13}\text{C}$ Urea Breath Test (Pylobactell®)</td>
<td></td>
</tr>
</tbody>
</table>

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**END**