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
^{13}C-urea	100 mg

For a full list of excipients, see section 6.1.

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

Pylobactell is not recommended for use in children below the age of 18 years due to insufficient data on efficacy.

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 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 Contraindications

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 listed in section 6.1.

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, 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 Fertility, 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.

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 appropriate national reporting system (see details below)

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL-Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517

Website: www.hpra.ie
e-mail: medsafety@hpra.ie

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 ^{13}C-urea is metabolised by the enzyme urease which is present in *H.pylori*.

$H_2N(^{13}CO)NH_2 + H_2O \rightarrow 2NH_3 + {}^{13}CO_2$

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 ≥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 (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 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 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 six hours prior to the test.

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

<u>Sampling instructions</u>

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.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

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 a 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 autosampler 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 CO_2 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 3SD'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. pylori status: -< 3.5 excess $\delta^{13}C$ = Negative
≥ 3.5 excess $\delta^{13}C$ = Positive

7. MARKETING AUTHORISATION HOLDER

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+44 (0)1953 713649
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8. MARKETING AUTHORISATION NUMBER

EU/1/98/064/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 07 May 1998
Date of latest renewal: 07 May 2008

10. DATE OF REVISION OF THE TEXT

03/2017

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.