**PYTEST- urea, c-14 capsule**
**Avent, Inc.**

---

## PYtest[1] Kit ($^{14}$C-Urea Breath Test)

### Description

PYtest[1] ($^{14}$C-Urea Breath Test) is a qualitative and non-invasive method for the diagnosis of *Helicobacter pylori (H.pylori)*. To detect *H.pylori*, $^{14}$C-urea supplied in a capsule is swallowed by the patient. If gastric urease from *H.pylori* is present, Urea is split to form $CO_2$ and $NH_3$. Ten minutes after the patient ingests the capsule, a breath sample is collected into a balloon. The breath sample is later transferred to collection fluid to trap the labeled $CO_2$. The liquid sample is then analyzed in a liquid scintillation counter.

The PYtest[1] Kit ($^{14}$C-Urea Breath Test) is designed for use with the PYtest[1] capsule, a gelatin capsule for oral administration containing 1 µCi of $^{14}$C labeled urea. The urea is adsorbed on sugar spheres and colored yellow with fluorescein.

---

1 Registered Trademark or Trademark of Kimberly-Clark Worldwide, Inc.

### Data on $^{14}$C-urea

Structural Formula ($^{14}$C-urea): $NH_2\ ^{14}CONH_2$

Radiation emission: beta-emission, 49 $keV_{mean,}$ 156 $keV_{max,}$ no other emissions

External emission: No external radiation hazard. Low-energy beta emissions only. Maximum range of 0.3 mm in water.

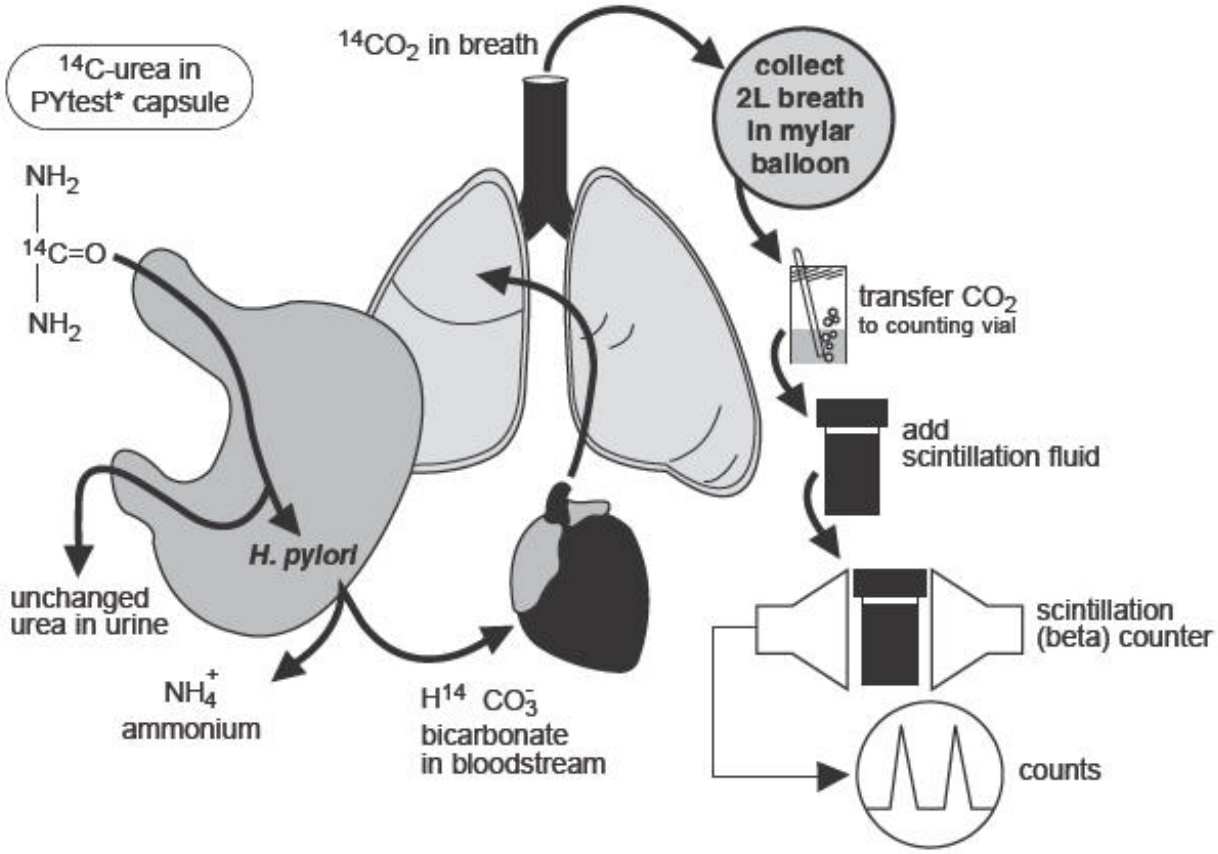
Radiological Half-life: 5730 years

Maximum effective dose equivalent (EDE) : 0.3 mrem/µCi

### Clinical Pharmacology

The urease enzyme is not present in mammalian cells, so the presence of urease in the stomach is evidence that bacteria are present. The presence of urease is not specific for *H.pylori*, but other bacteria are not usually found in the stomach. The principle of the breath test is shown in Figure 1.

**Figure 1: Principle of Breath Test**




To detect *H.pylori*, urea labeled with $^{14}C$ is swallowed by the patient. If gastric urease from *H.pylori* is present, urea is split to form $CO_2$ and $NH_3$ at the interface between the gastric epithelium and lumen and $^{14}CO_2$ is absorbed into the blood and exhaled in the breath.

Following ingestion of the capsule by a patient with *H.pylori*, $^{14}CO_2$ excretion in the breath peaks between 10 and 15 minutes and declines thereafter with a biological half-life of about 15 minutes. $^{14}C$-urea that is not hydrolyzed by *H.pylori* is excreted in the urine with a half-life of approximately 12 hours. About 10% of the $^{14}C$ remains in the body at 72 hours and is gradually excreted with a biological half-life of 40 days.

**Clinical Studies**

Two studies were performed. In both studies, patients with gastrointestinal symptoms underwent the breath test and an endoscopy. During the endoscopy, biopsy samples were taken from the antral gastric mucosa for histological analysis (2 samples, Giemsa stain) and rapid urease test (1 sample, CLOtest[1]). Breath samples were mailed to the TRI-MED lab where they were read in a liquid scintillation counter.

Results were reported as disintegrations per minute (DPM). Analysis for accuracy used the ten minute breath sample. A breath sample DPM <50 was defined as a negative result. DPM ≥200 was defined as a positive result. DPM in the range of 50 -199 was classified as indeterminate.

**STUDY 1**

Of 186 patients who had histopathology and CLOtest[1] (80 men, 106 women), 53 were infected with *H.pylori* as determined by agreement between histology and CLOtest[1]. The study results are summarized below:

**Table 1: Study #1 (n=186, Indeterminate results included)**

| | **Histology and CLOtest[1]** |
|---|---|

| | *H.pylori* | Positive | Negative | Total | |
|---|---|---|---|---|---|
| PYtest[1] | Positive | 51 | 8 | 59 | ppv. 86% |
| (DPM | Indeterminate | 1 | 8 | 9 | |
| 10m.) | Negative | 1 | 117 | 118 | npv. 99% |
| | Total | 53 | 133 | 186 | |
| | | sensitivity 96% | specificity 88% | | |

**Notes:** *PYtest[1] at 10 min. was compared to the gold standard of biopsy results in which histology and CLOtest[1] concurred. Patients who did not have both biopsy tests performed, or in whom the tests differed, were excluded from analysis. There was no statistical difference in test accuracy based on gender of patient.*

***ppv = positive predictive value (true positive divided by total PYtest[1] positive)***

***npv = negative predictive value (true negative divided by total PYtest[1] negative)***

**STUDY 2**

Breath tests were performed on 436 outpatients attending gastroenterology practices at sites in the United States. Seventy-six patients (40 men, 36 women) who had histology and CLOtest[1] were evaluated. The results are summarized below:

**Table 2: Study #2 (n=76, Indeterminate results included)**

| | | Histology and CLOtest[1] | | | |
|---|---|---|---|---|---|
| | *H.pylori* | Positive | Negative | Total | |
| PYtest[1] | Positive | 22 | 0 | 22 | ppv. 100% |
| (DPM | Indeterminate | 4 | 2 | 6 | |
| 10m.) | Negative | 1 | 47 | 48 | npv. 98% |
| | Total | 27 | 49 | 76 | |
| | | sensitivity 82% | specificity 96% | | |

**Notes:** *PYtest[1] at 10 min. was compared to the gold standard of biopsy results in which histology and CLOtest concurred. Patients who did not have both biopsy tests performed, or in whom the tests differed, were excluded from analysis. There was no statistical difference in test accuracy based on gender of patient.*

***ppv = positive predictive value (true positive divided by total PYtest[1] positive)***

***npv = negative predictive value (true negative divided by total PYtest[1] negative)***

**Indications and Usage**

PYtest[1] ($^{14}$C-Urea Breath Test) is indicated for use in the detection of gastric urease as an aid in the diagnosis of *H.pylori* infection in the human stomach. The test utilizes a liquid scintillation counter for the measurement of $^{14}CO_2$ in breath samples.

**Contraindications**

None

## Warnings

None

## Precautions

### General

After the patient ingests the $^{14}$C-urea capsule, the sample collected for test purposes is for in vitro diagnostic use only.

A false positive test could occur in patients who have achlorhydria. Very rarely, a false positive test may occur due to urease associated with Helicobacters other than *H.pylori* (i.e. *Helicobacter heilmanni*).

### Limitations of the Test

- The test has been evaluated in outpatients before elective endoscopy.
- Test results should be evaluated with clinical signs and patient history when diagnosing *H.pylori* infection.
- The performance characteristics of the test have not been established for monitoring the efficacy of antimicrobial therapies for the treatment of *H.pylori* infection.
- A negative result does not completely rule out the possibility of *H.pylori* infection. If clinical signs and patient history suggest *H.pylori* infection, repeat the PYtest[1] or use an alternative diagnostic method.
- The integrity of samples in balloons sent by air transport has not been adequately determined. In studies simulating the effects of air transport for two to seven days at temperatures of -40°C, 20°C and 55°C, no balloon failures were observed. However, the data could not provide statistical determination that no changes in $^{14}CO_2$ concentration took place.
- For ground transport, integrity of samples in balloons has not been determined beyond 7 days. During this time frame, concentration of labeled $CO_2$ can decrease as much as 0.36% per day.

### Radioactivity

Persons concerned about very low doses of radioactivity may postpone the test or may decide to use an alternative means of diagnosis. The test produces radiation exposure equal to 24 hours of normal background. In animal experiments, such low doses of radiation do not carry measurable risk.

Preclinical studies were not conducted on $^{14}$C-urea. The estimated dose equivalent received from a single administration of PYtest[1] (1µCi $^{14}$C) is about 0.3 mrem.

### Information for Patients

It is necessary for the patient to fast for 6 hours before the test. The patient should also be off antibiotics and bismuth for 1 month, and proton pump inhibitors and sucralfate for 2 weeks prior to the test. Instruct the patient not to handle the capsule directly as this may interfere with the test result. The capsule should be swallowed intact. Do not chew the capsule.

### Carcinogenesis, mutagenesis, impairment of fertility

No studies have been conducted with $^{14}$C-urea to evaluate its potential for carcinogenicity, impairment of fertility, or mutagenicity.

### Drug Interactions

Antibiotics, proton pump inhibitors, sucralfate, and bismuth preparations are known to suppress H.pylori. Ingestion of antibiotics or bismuth within 4 weeks and proton pump inhibitors or sucralfate within 2 weeks prior to performing the test may give false negative results.

**Pregnancy**

Pregnancy category C

Animal reproduction studies have not been conducted with PYtest[1] ($^{14}$C-urea). It is also not known whether PYtest[1] can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. PYtest[1] should be given to a pregnant woman only if clearly needed.

**Nursing mothers**

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when PYtest[1] is administered to a nursing woman.

**Pediatric Use**

Clinical studies in children have not been conducted. However, PYtest[1] is expected to work the same in children as in adults. While the dose (1 capsule) does not need to be adjusted, the child must be able to swallow the intact capsule and blow into a straw.

**Adverse Reactions**

No adverse reactions were reported in clinical trials.

**Overdosage**

Risk from radiation is negligible even with a 1000 capsule overdose (0.3 rem). If overdose occurs, the patient may drink one glass of water (150 mL) every hour to hasten excretion of the isotope. Maximum excretion of Urea is achieved at a urine output of ≥2.0 mL/min.

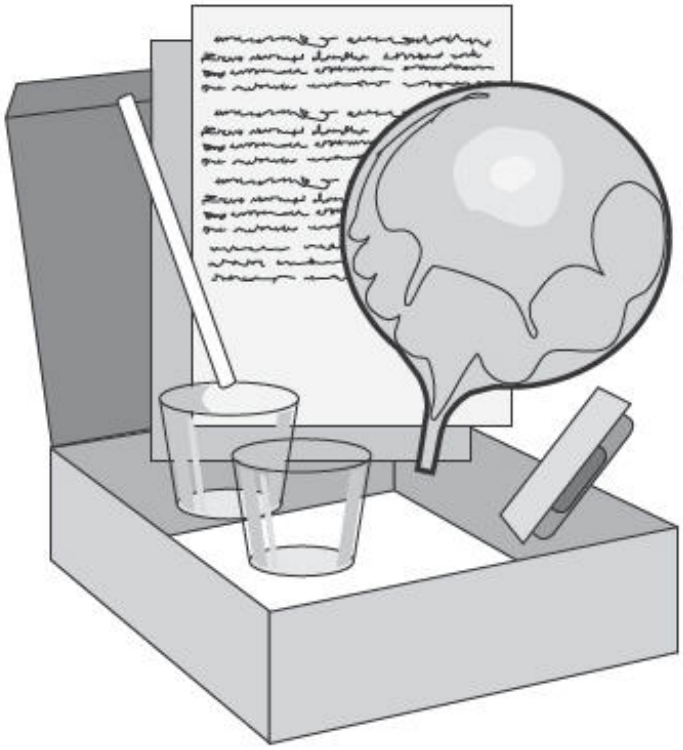
**Dosage and Administration**

**Materials provided**

As shown in Figure 2, the PYtest[1] Kit contains:

- PYtest[1] capsule
- Two 30 mL disposable cups
- One drinking straw
- One mylar collection balloon
- One report form
- One mailing box with labels[2]

**Figure 2: PYtest[1] Kit**



[2] **The kit includes analysis by Kimberly-Clark of one balloon from one patient at one time point.**

### Materials Needed but not Provided

1. Stopwatch/Timer capable of timing an interval up to 10 minutes.
2. Water (40mL)

### Dosage

One PYtest[1] capsule.

### Procedural Notes

- Inform the patient to fast for 6 hours prior to the test.
- The patient should be off antibiotics and bismuth for 1 month, and proton pump inhibitors and sucralfate for 2 weeks prior to the test.
- Have patient sitting at rest while doing the test.
- The capsule should not be handled directly as this may interfere with the test result.
- To avoid contamination by bacteria in the mouth, the capsule should be swallowed intact. Do not chew capsule.

### Step by Step Procedure for Balloon

**Table 3: Breath Sample Collection by Balloon**

| | |
|---|---|
| Before the test | 1. Label balloon and fill in breath test report form.<br>2. Check that all materials are present. |
| Minus 1 | 1. Open the package containing the $^{14}$C-urea capsule minute and tip the capsule into the empty 30 mL cup. Do not handle the capsule directly.<br>2. Hand the cup to the patient. |

| | |
|---|---|
| | 3. Fill the second cup with 20 mL lukewarm water. |
| 0 minute | 1. Ask the patient to tip the capsule directly into his/her mouth, then swallow it with the 20 mL of lukewarm water.<br>2. Start the stopwatch when the patient swallows the capsule.<br>3. Discard waste (e.g., capsule packaging, used straws) according to your facility's regulations. |
| 3 minutes | Ask the patient to drink another 20 mL of lukewarm water (in case the capsule may have lodged in the esophagus and not yet reached the gastric mucosa). |
| 10 minutes | 1. Push a drinking straw into the neck of the balloon.<br>2. Ask the patient to hold his/her breath for 5-10 seconds, then blow up a balloon with a slow breath through the straw, filling the balloon completely.<br>3. Tie the neck of the balloon into a tight knot.<br>4. Check that the balloon label and the breath test report form are completed correctly. |
| After the test | Place the filled balloon and breath test report in the box and forward to Kimberly-Clark for analysis. |

**Quality Control**

A minimum of 1 mM of $CO_2$ is required to perform analysis of a breath sample. The amount of breath required to provide 1 mM of $CO_2$ varies depending on the amount of $CO_2$ the patient is producing. Since a full balloon typically contains at least 1 mM of $CO_2$, the balloon should be completely filled.

**Results**

| ***Interpretation of results (10 minute sample)*** | |
|---|---|
| <50 DPM | Negative for *H.pylori* |
| 50-199 DPM | Indeterminate for *H.pylori* |
| ≥200 DPM | Positive for *H.pylori* |

The indeterminate result should be evaluated by repeating the PYtest[1] or using an alternative diagnostic method. If repeat breath testing is undertaken, careful history to exclude confounding factors should be obtained. If confounding factors are present, wait an appropriate time (refer to Table 4) before repeating the PYtest[1].

The cutoff point of 50 DPM was determined to be the mean + 3SD of results obtained in patients who did not have *H.pylori*.

DPM = Disintegrations per minute

**Table 4: Factors which might cause sub-optimal breath test results**

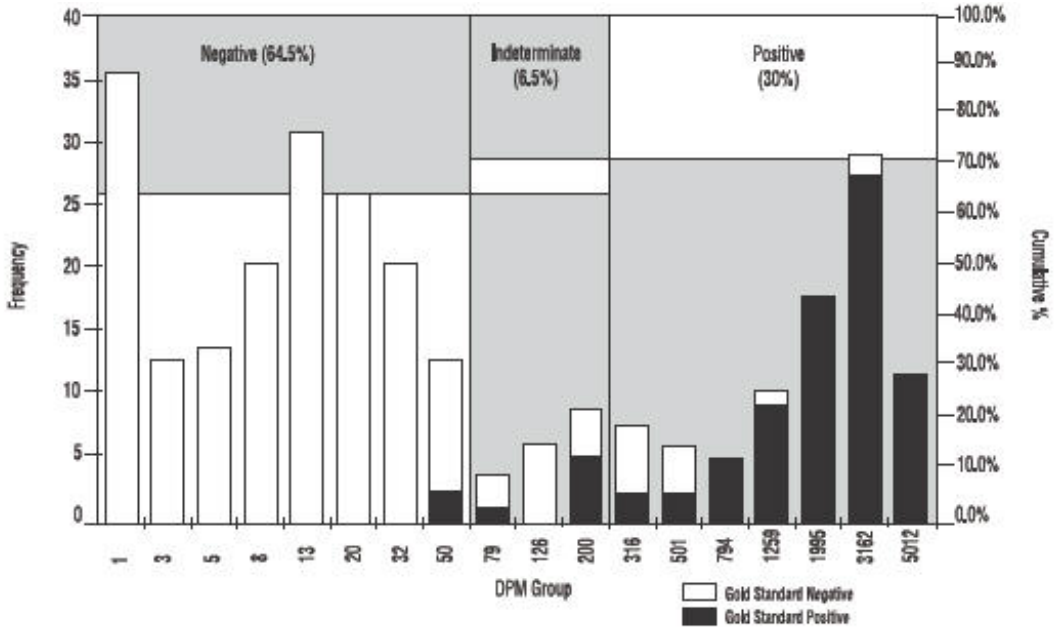
| Factor | Result | Comment |
|---|---|---|
| Recent antibiotic or bismuth (Pepto-Bismol, etc.) | false neg. | Relapse of partially treated *Hp* may take 1-4 weeks. |
| Omeprazole (or other proton pump inhibitors) | false neg. | These agents suppress *Hp* in 40% of patients. Discontinue for at least 2 weeks before performing the |

| | | |
|---|---|---|
| | | PYtest[1]. |
| Resective gastric surgery | false neg. | Isotope may empty rapidly from the stomach. |
| Resective gastric surgery | false pos. | Patient may be achlorhydric and have bacterial overgrowth (non-*Hp* urease). |
| Food in stomach (also bezoar, gastroparesis) | unknown | Isotope may not come into contact with gastric mucosa. Patient may be achlorhydric and/or have bacterial overgrowth (non-*Hp* urease). |

**Expected Values**

As shown in Figure 3 approximately 30% of patients tested will be positive for *H.pylori.*

**Figure 3: Histogram showing DPM distribution for the PYtest[1].**




***Note:*** *DPM groupings were calculated on a logarithmic scale. Empty DPM groupings were not included. Chart includes all patients from Studies 1 and 2.*

*Frequency of DPM group includes samples with DPM < Group Name.*

**DPM = Disintegrations per minute**

**Gold Standard = Agreement between histology and CLOtest[1]**

If the capsule is damaged or appears abnormal in any way, it may give inaccurate results.

**How Supplied**

PYtest[1] Kit ($^{14}$C-Urea Breath Test) is supplied as a kit containing a PYtest[1] Capsule, a clear gelatin capsule containing 1µCi of $^{14}$C-urea and breath collection equipment.

PYtest[1] Capsules are also supplied separately in unit dose packages of 1,10 and 100.

The PYtest[1] Capsule has a shelf life of two years. The expiration date is printed on the capsule label.

PYtest[1] Capsules and Kit should be stored at 15°-30°C (59°-86°F) in an area designated by each individual institution's regulations.

**Rx Only**

**Kimberly-Clark** Distributed in the U.S. by Kimberly-Clark Global Sales, LLC,
Roswell, GA 30076 USA
**In USA, please call 1-800-KCHELPS • www.kchealthcare.com**
Kimberly-Clark, Roswell, GA 30076 USA
Kimberly-Clark N.V., Belgicastraat 13, 1930 Zaventem, Belgium
Sponsored in Australia by Kimberly-Clark Australia Pty Limited; 52 Alfred Street,
Milsons Point, NSW 2061 • 1-800-101-021


14-63-136-0-00/70080910 12/07

**PRINCIPAL DISPLAY PANEL - PYtest* Kit Label**

**HALYARD***

**PYtest* KIT**
**$^{14}$C-UREA BREATH TEST FOR THE DETECTION OF *HELICOBACTER PYLORI***

**Contents – 1 PYtest* Capsule each containing 1 µCi $^{14}$C-Urea**
**PYtest* Breath Collection Accessories**
**$^{14}$C-Urea (5730 years1/2, 156 keV$_{[max.]}$ β-emission)**
**For dosage information, please see package insert**

**This package conforms to the conditions and limitations specified in 49 CFR 173.421 for radioactive material, excepted package-limited quantity of material, UN 2910.**

**For In Vitro Diagnostic Use**
**Rx Only**
**Store at 15°–30°C (59°–86°F)**

**Distributed in the USA by Halyard Sales, LLC, Alpharetta, GA 30004; In USA, please call 1-844-425-9273 • halyardhealth.com**
**Halyard Health, Inc., 5405 Windward Parkway, Alpharetta, GA 30004 USA EC|REP Haylyard Belgium BVBA, Leonardo Da Vincilaan 1,**
**1930 Zaventem, Belgium; Sponsored in Australia by Halyard Australia Pty Limited; 52 Alfred Street, Milsons Point, NSW 2061**

HALYARD

# PYtest* KIT

## $^{14}$C-UREA BREATH TEST FOR THE DETECTION OF *HELICOBACTER PYLORI*

Contents – 1 PYtest* Capsule each containing 1 µCi $^{14}$C-Urea
PYtest* Breath Collection Accessories
$^{14}$C-Urea (5730 years1/2, 156 keV$_{[max.]}$ ß-emission)
For dosage information, please see package insert

This package conforms to the conditions and limitations specified in 49 CFR 173.421 for radioactive material, excepted package-limited quantity of material, UN 2910.

| For In Vitro Diagnostic Use | Rx Only | Store at 15°–30°C (59°–86°F) |
|---|---|---|



# PYTEST

urea, c-14 capsule

## Product Information

| | | | |
|---|---|---|---|
| **Product Type** | HUMAN PRESCRIPTION DRUG | **Item Code (Source)** | NDC:42536-6046 |
| **Route of Administration** | ORAL | | |

## Active Ingredient/Active Moiety

| Ingredient Name | Basis of Strength | Strength |
|---|---|---|
| **Urea C-14** (UNII: WBZ6M63TEE) (Urea C-14 - UNII:WBZ6M63TEE) | Urea C-14 | 1 uCi |

## Product Characteristics

| | | | |
|---|---|---|---|
| **Color** | YELLOW (Light Lemon Yellow) | **Score** | no score |
| **Shape** | CAPSULE (Oval) | **Size** | 15mm |
| **Flavor** | | **Imprint Code** | |
| **Contains** | | | |

## Packaging

| # | Item Code | Package Description | Marketing Start Date | Marketing End Date |
|---|---|---|---|---|
| **1** | NDC:42536-6046-1 | 1 in 1 PACKAGE, COMBINATION | | |
| **1** | | 1 in 1 BLISTER PACK; Type 0: Not a Combination Product | | |
| **2** | NDC:42536-6046-2 | 10 in 1 PACKAGE, COMBINATION; Type 0: Not a Combination Product | | |
| **3** | NDC:42536- | 100 in 1 PACKAGE, COMBINATION; Type 0: Not a Combination | | |

| | | | | |
|---|---|---|---|---|
| 3 | 6046-3 | Product | | |

## Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|---|---|---|---|
| NDA | NDA020617 | 05/09/1997 | |

## Labeler - Avent, Inc. (049316284)

Revised: 3/2016 Avent, Inc.