Ingestible pH and Pressure Capsule

Policy Number: 2.01.81  Last Review: 5/2015

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for ingestible pH and pressure capsule. This is considered investigational.

When Policy Topic is covered
Not Applicable

When Policy Topic is not covered
Measurement of gastrointestinal transit times, including gastric emptying and colonic transit times, using an ingestible pH and pressure capsule is considered investigational for the evaluation of suspected gastroparesis, constipation, or other gastrointestinal motility disorders.

Description of Procedure or Service
An ingestible pH and pressure-sensing capsule (SmartPill® GI Monitoring System) measures pH, pressure, and temperature changes to signify passage of the capsule through portions of the gastrointestinal tract. It is proposed as a means of evaluating gastric emptying for diagnosis of gastroparesis, and colonic transit times for the diagnosis of slow-transit constipation.

Available studies provide some information regarding the comparison of the SmartPill ingestible pH and pressure-sensing capsule to other techniques for measuring gastric emptying and whole-gut transit times, but this evidence primarily consists of concordance with available tests. Because the available tests, such as nuclear scintigraphy, are imperfect criterion standards, it is not possible to determine the true sensitivity and specificity of SmartPill. The results of the concordance studies reveal a moderate correlation with alternative tests but provide only limited further information on the true accuracy of the test in clinical care. Evaluation of cases with discordant results would be of particular value, and ideally, these studies should be linked to therapeutic decisions and to meaningful clinical outcomes. The evidence to date on clinical utility of testing is lacking, consisting of a small number of retrospective studies. This does not provide sufficient information to determine whether health outcomes are improved as a result of the information provided by the SmartPill. Because the impact of this technology on net health outcome is unknown, this technology is considered investigational.

Background
Gastroparesis is a chronic disorder characterized by delayed gastric emptying in the absence of mechanical obstruction. Symptoms of gastroparesis are often nonspecific and may mimic other gastrointestinal tract disorders. It can be caused by many conditions; most commonly it is idiopathic, diabetic, or postsurgical.

The test considered the reference standard for gastroparesis is called gastric emptying scintigraphy. The patient ingests a radionuclide-labeled standard meal, and then images are performed at 0, 1, 2, and 4 hours postprandially to measure how much of the meal has passed beyond the stomach. A typical threshold to indicate abnormal gastric emptying is more than 10% of the meal remaining at 4 hours after ingestion.
Constipation is a chronic disorder involving infrequent bowel movements, sensation of obstruction, and incomplete evacuation. Many medical conditions can cause constipation such as mechanical obstruction, metabolic conditions, myopathies, and neuropathies. Diagnostic testing for constipation can aid in distinguishing between two categories of disorders, slow-transit constipation and pelvic floor dysfunction.

Standard tests used in the evaluation of constipation include ingestion of radio-opaque markers and colonic transit scintigraphy. In the radio-opaque markers test, small markers are ingested over one or several days, and abdominal x-rays are performed at 4 and/or 7 days. The number of remaining markers correlates with the colonic transit time. In colonic transit scintigraphy, a radio-labeled meal is ingested, followed by scintigraphic imaging at several time intervals. The location of the scintigraphic signals correlates with colonic transit times.

In 2006, an ingestible capsule (SmartPill® GI Monitoring System) was cleared for marketing by the U.S. Food and Drug Administration (FDA) via a 510(k) application, with the indication for use to evaluate delayed gastric emptying. Gastric emptying is signaled when the pH monitor in the capsule indicates a change in pH from the acidic environment of the stomach to the alkaline environment of the small intestine. While SmartPill does not measure 50% emptying time, it can be correlated with scintigraphically measured 50% emptying time. The capsule also measures pressure and temperature throughout its transit through the entire gastrointestinal tract, allowing calculations of total GI transit time. In 2009, the FDA expanded the use of the SmartPill to determine colonic transit time for the evaluation of chronic constipation and to differentiate between slow versus normal transit constipation. When colonic transit time cannot be determined, small and large bowel transit times combined can be used instead. The SmartPill is not for use in pediatric patients.

The ingestible pH and pressure capsule (i.e., SmartPill®) measures pH, pressure, and temperature changes to signify passage of the capsule through portions of the gastrointestinal tract. For example, an increase of 2 or more pH units usually indicates gastric emptying, and a subsequent decrease of 1 or more pH units usually indicates passage to the ileocecal junction. This differs from esophageal pH monitoring for gastroesophageal reflux disease, which measures pH levels in various ways such as through catheters, impedance or a temporarily implanted device such as the Bravo. The ingestible pH and pressure capsule (i.e., SmartPill®) also differs from the wireless capsule endoscopy (i.e., PillCam™), which is a capsule swallowed by the patient that transmits video images wirelessly.

**Rationale**

This policy was originally created in 2009 and was updated regularly with searches of the MEDLINE database. The most recent literature review was performed through February 18, 2014. Following is a summary of the key literature to date.

Evaluation of a diagnostic technology typically focuses on the following 3 parameters: (1) technical performance; (2) diagnostic parameters (sensitivity, specificity, positive and negative predictive value) in different populations of patients; and (3) demonstration that the diagnostic information can be used to improve patient outcomes. Additionally, when considering invasive monitoring, any improvements in patient outcomes must be outweighed by device-related risks associated with testing.

**Diagnostic Accuracy of Wireless Pressure and pH Capsule**

**Gastric Emptying**

Although gastric emptying scintigraphy is considered the reference standard for evaluating gastric emptying, several issues complicate its use as a reference test. Until recently, there has been a lack of standardization of the test. Differences in the test meal used, patient positioning, frequency, duration, and interpretation of imaging all limit the clinical utility of the test. Significant day-to-day variability in the rate of gastric emptying has been noted.
There is limited knowledge regarding the capability of the gastric emptying test to discriminate between healthy individuals and those with known gastroparesis due to lack of standardization of the test and small patient samples in published studies. A 2000 study, which proposed a threshold of normality at 10% meal retention at 4 hours, included only 123 healthy subjects.(3) The cutoff point was set to include 95% of normal persons. However, it appears to be unknown if this same threshold adequately identifies persons who would otherwise be classified as having gastroparesis and who are candidates or responders to treatment.

There are few published studies that evaluate the ingestible capsule in relation to another measure of gastric emptying. A 2013 systematic review of 12 studies on the ingestible capsule was published by the Agency for Healthcare Research and Quality (AHRQ).(4) While studies that included only healthy participants were excluded from the AHRQ review, studies were included that used comparison groups consisting of healthy, asymptomatic (ie, without symptoms of gastroparesis or constipation) participants as controls, thus limiting interpretation of the comparisons. Overall, the strength of evidence in the available studies on the ingestible capsule was found to be low. Diagnostic accuracy with the ingestible capsule was considered comparable with gastric scintigraphy in 7 studies with diagnostic agreement ranging from 58% to 86% for test agreement when test results were positive and 64% to 81% when results were negative. There was moderate correlation between the ingestible capsule and gastric emptying scintigraphy on transit data and device agreement in 5 studies. Three studies that evaluated transit time reported similar sensitivity and specificity for the ingestible capsule and scintigraphy.

Cassily et al (2008) evaluated the SmartPill and simultaneous gastric emptying scintigraphy in 15 healthy subjects.(5) The capsule was ingested immediately after ingesting the radiolabeled test meal. In this study, the mean time for 50% gastric emptying by scintigraphy was 95 minutes, 90% gastric emptying by scintigraphy was 194 minutes, and gastric residence time by SmartPill was 261 minutes. The correlation of SmartPill to 50% gastric emptying time was r=0.606 and to 90% gastric emptying time was r=0.565. The average amount of meal remaining in the stomach at the time the SmartPill exited the stomach was 5.4%. This study showed only modest correlation of the SmartPill and gastric emptying scintigraphy. The study is too small to establish reference values for the SmartPill.

In a 2008 study by Kuo et al, 87 healthy subjects and 61 subjects with symptoms and prior positive test results for gastroparesis were evaluated with both the SmartPill and gastric emptying scintigraphy.(6) In this study, subjects ingested the capsule just before ingesting the standard meal. This resulted in 5 subjects who passed the SmartPill in less than 30 minutes, who were then subsequently considered to have invalid tests. Sixteen other subjects had equipment malfunctions, and 2 others dropped out.

Among the remaining 125 subjects, the correlation of SmartPill emptying time and scintigraphy at 2 hours was r=0.63, and between SmartPill emptying time and scintigraphy at 4 hours was r=0.73. In terms of the capability to discriminate between gastroparetic patients and healthy subjects, the area under the curve was 0.83 for SmartPill, 0.82 for scintigraphy at 4 hours, and 0.79 for scintigraphy at 2 hours (all p>0.05 for statistical significance), indicating similar capability for discriminating between the two patient groups. At a cutoff point of 300 minutes for the SmartPill, which was established by calculating the ideal cutoff point from the data, sensitivity was 65% and specificity was 87%. Sensitivity and specificity for scintigraphy using an established cutoff point from the literature of 10% at 4 hours was 44% and 93%, respectively.

In terms of adverse events reported in the study by Kuo et al, 5 (7%) of 67 subjects who did not retrieve the capsule required a second additional plain radiograph (x-ray) beyond 5 days to demonstrate that the capsule had been passed.(6) Another patient had ingested a laxative that caused the capsule to be entrapped in a viscous mass. An unsuccessful endoscopy and treatment with intravenous erythromycin was required to pass the capsule from the stomach.

A 2009 study by Maqbool et al assessed SmartPill and gastric emptying scintigraphy in 10 healthy asymptomatic subjects.(7) Emptying time assessed by SmartPill was correlated with the percent meal
retained at 2 and 4 hours. The correlation between SmartPill and 2-hour scintigraphy was $r=0.95$. The correlation between SmartPill and 4-hour scintigraphy was $r=0.73$.

**Section Summary**

These data have several shortcomings regarding the use of the SmartPill in diagnosing gastroparesis, and as a result, the diagnostic accuracy is not well defined. The current reference test, scintigraphy, is an imperfect criterion standard, and this creates difficulties in defining the sensitivity and specificity of SmartPill. All of the studies include healthy asymptomatic subjects either entirely or as part of a control group. Healthy subjects do not represent the clinically relevant group under consideration for a diagnosis of delayed gastric emptying. The relevant population of subjects should have symptoms or are being considered for the diagnosis of gastroparesis. Although there was moderate correlation between SmartPill gastric emptying time and scintigraphy, scintigraphy itself has limited reliability. Although overall, the AUCs between SmartPill and scintigraphy are similar, the modest correlation between the 2 tests means that there are often discordant results. What such discordant results mean in terms of diagnosis and treatment are uncertain.

**Colon Transit Time**

Few studies evaluate the use of SmartPill for evaluating colonic transit times. In a 2013 systematic review by Agency for Healthcare Research and Quality (AHRQ), the strength of evidence in available studies on the ingestible capsule was found to be low overall. (4) Accuracy of the ingestible capsule in diagnosing slow-transit constipation was similar to tests using radiopaque markers and scintigraphy. Moderate correlation between colon transit times with the ingestible capsule and tests with radiopaque markers was shown in 5 studies with correlation coefficients ranging from 0.69 to 0.71.

In the 2009 study by Maqbool et al referred to earlier, healthy asymptomatic subjects underwent simultaneous whole-gut scintigraphy and SmartPill assessment of whole gut transit times. (7) The 2 techniques correlated with each other reasonably well. In a 2009 study by Rao et al, normal subjects and subjects with constipation had whole gut transit times assessed with radio-opaque markers and the SmartPill. (8) Diagnostic accuracy of the 2 techniques in differentiating the 2 groups of patients was similar. Camilleri et al (2010) compared the wireless motility capsule with radio-opaque markers in 158 patients with chronic functional constipation. (9) In this multicenter validation study, the authors reported that positive percent agreement between the wireless motility capsule and radio-opaque markers was approximately 80% for colon transit time (95% confidence interval [CI], 0.67 to 0.98) and small and large bowel transit time (95% CI, 0.67 to 0.89). No serious adverse events occurred in the study.

FDA has received 1 adverse event report according to their MAUDE (Manufacturer and User Facility Device Experience) database, in which the capsule was trapped in the stomach of a patient and required endoscopic removal.

**Section Summary**

Although these studies show moderate correlations between SmartPill and other methods for assessing colonic transit times, the studies have several shortcomings. Two of the studies included healthy subjects, who are not the appropriate subjects for evaluating a diagnostic test. The studies did not identify a set of subjects with known slow-transit constipation, which is the clinically relevant subset of patients with constipation that the test should identify. Thus, the diagnostic characteristics of SmartPill for detecting slow-transit constipation are unknown.

**Clinical Utility of Wireless Pressure Capsule**

Demonstration of clinical utility requires that the technology be associated with change(s) in management that lead to improved health outcomes.

The 2013 systematic review by AHRQ found that there was limited evidence available on the clinical impact of testing with the ingestible capsule. (4) Therefore, the evidence was insufficient to draw conclusions regarding the impact of ingestible capsule testing results on treatment and management decisions.
In a retrospective study of 83 patients evaluated for gastroparesis, small intestinal dysmotility, and constipation, Kuo et al (2011) found wireless motility capsule testing resulted in a new diagnosis in 44 patients (53%).(10) Clinical management changes were recommended in 65 patients. These included changes in medication regimens in 39 patients (60%) and in nutrition programs in 9 patients (14%). Four patients (6%) were referred to surgery for colectomy. Abnormal gastric emptying or small intestinal transit times did not influence patient management at all (p=NS). Abnormal colon transit times did not influence nutritional program changes (p=0.72) but did influence medication changes (p=0.02) and resulted in a trend toward increased surgical referrals (p=0.12). The authors believe wireless motility capsule testing eliminated the need for nuclear gastric emptying testing in 9 (17%) of 52 patients, barium radiography testing in 7 (54%) of 13 patients, and radio-opaque marker testing in 41 (68%) of 60 patients. The authors noted a need for prospective studies to further understand wireless motility capsule testing and its role in patient management.

In a retrospective study of 86 patients with persistent symptoms of gastrointestinal dysmotility, despite normal endoscopic and radiologic test results, Rao et al (2011) found that evaluations with wireless motility capsule testing resulted in new diagnostic information in 26 (53%) of 50 patients with lower gastrointestinal symptoms and 17 (47%) of 36 patients with upper gastrointestinal symptoms.(11) Clinical management was influenced by wireless motility capsule testing in 30% of patients with lower gastrointestinal symptoms and in 50% of patients with upper gastrointestinal symptoms. The retrospective nature of this study limits interpretation of results.

Section Summary
Evidence on the clinical utility of wireless pressure capsule is very limited, consisting of 2 retrospective analyses. This evidence is insufficient to determine the clinical utility of SmartPill; further higher quality studies are needed on the impact of SmartPill on patient management.

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov on February 6, 2015 identified 1 ongoing clinical trial evaluating the diagnostic accuracy and/or clinical validity of an ingestible pH and pressure capsule:

Clinical Management With SPM (SmartPill Monitoring) System and Validation of the SPM 5 Hour Cutoff in Patients With Symptoms of Gastroparesis (NCT02022826): In this industry-sponsored trial, patients with gastroparesis for at least 12 weeks will undergo concurrent gastric scintigraphy and SmartPill monitoring. The primary study outcomes are per patient agreement between gastric emptying time with the 2 tests and per patient agreement for the diagnosis of delayed gastric emptying time. The estimated date of study completion is July 2016.

Summary of Evidence
Available studies provide some information regarding the comparison of the SmartPill ingestible pH and pressure-sensing capsule to other techniques for measuring gastric emptying and whole-gut transit times, but this evidence primarily consists of concordance with available tests. Because the available tests, such as nuclear scintigraphy, are imperfect criterion standards, it is not possible to determine the true sensitivity and specificity of SmartPill. The results of the concordance studies reveal a moderate correlation with alternative tests but provide only limited further information on the true accuracy of the test in clinical care. Evaluation of cases with discordant results would be of particular value, and ideally, these studies should be linked to therapeutic decisions and to meaningful clinical outcomes. The evidence to date on clinical utility of testing is lacking, consisting of a small number of retrospective studies. This does not provide sufficient information to determine whether health outcomes are improved as a result of the information provided by the SmartPill. Because the impact of this technology on net health outcome is unknown, this technology is considered investigational.

Practice Guidelines and Position Statements
The American Neurogastroenterology and Motility Society issued a consensus statement on intraluminal measurement of gastrointestinal and colonic motility in clinical practice in 2008.(12) In this consensus statement, formal recommendations regarding any type of test are not issued. It is
mentioned that SmartPill can be used to identify delayed gastric emptying, but that the impact of the technology on management of patients has not been studied. Use of SmartPill to assess colonic motility is noted, but no mention is made of its use to measure colonic transit time.

The American and European Neurogastroenterology and Motility Societies issued a position paper on gastrointestinal transit evaluation in 2011.(13) In this position paper, the wireless motility capsule is recommended by consensus for assessing gastric emptying, small bowel, colonic, and whole-gut transit times in patients with suspected gastroparesis or gastrointestinal dysmotility in multiple regions. However, the position paper notes the clinical utility of identifying delays in small bowel transit times is unknown.

The American Gastroenterological Association’s 2013 guidelines on gastroparesis diagnosis and treatment indicate wireless motility capsule testing requires validation before it can be considered as an alternative to scintigraphy for diagnosing gastroparesis.(14) Gastric emptying scintigraphy is considered the best accepted method to test for delays in gastric emptying.

The American College of Gastroenterology’s 2013 guideline on the management of gastroparesis stated that wireless capsule motility testing and 13C breath testing require further validation before they can be considered alternates. (Conditional recommendation, moderate level of evidence).(15)

**Medicare National Coverage**

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

**References:**


**Billing Coding/Physician Documentation Information**

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<td>91112</td>
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Category III code, 0242T Gastrointestinal transit and pressure measurement, stomach through colon, wireless capsule, with interpretation and report was deleted effective 12/31/2012 and replaced with a category I CPT code (91112).

**Additional Policy Key Words**

N/A

**Policy Implementation/Update Information**

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<td>5/1/11</td>
<td>No policy statement changes. Coding updated.</td>
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<td>5/1/12</td>
<td>Policy statement revised to include measurement of whole gut transit time and evaluation of gut motility disorders other than gastroparesis.</td>
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