Effective February 26, 2018
Policy Replaced by LCD L33455

BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Ingestible pH and Pressure Capsule

Policy #: 379
Category: Medical

Latest Review Date: December 2017
Policy Grade: B

Background:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*

    - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
    - *Furnished in a setting appropriate to the patient's medical needs and condition;*
    - *Ordered and furnished by qualified personnel;*
    - *One that meets, but does not exceed, the patient's medical need; and*
    - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

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.

Gastroparesis and Constipation

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 disorders. It can be caused by many conditions; most commonly it is idiopathic, diabetic or post-surgical.

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.

Diagnosis

Gastric emptying scintigraphy is considered the reference standard for diagnosing gastroparesis. The patient ingests a radionuclide-labeled standard meal, and then images are performed at zero, one, two, and four 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 four hours after ingestion.

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 four and/or seven 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.

Policy:

Effective for dates of service on or after October 3, 2009 and prior to February 26, 2018:
Blue Advantage will treat **measurement of gastrointestinal transit times, including gastric emptying and colonic transit times, gastric emptying using an ingestible pH and pressure capsule (SmartPill® GI Monitoring System)** as a **non-covered** benefit and as **investigational** for the evaluation of suspected gastroparesis, constipation or other gastrointestinal motility disorders.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians

should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The most recent literature review was updated through September 14, 2017.

Wireless pH and Pressure Capsule

Technical Reliability

We did not identify any literature assessing the technical reliability of wireless pH pressure capsules.

Clinical Validity

Gastric Emptying

Although 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. The clinical utility of the test depends on the frequency, duration, and interpretation of imaging and is affected by factors including the use of different test meals and patient positioning. Significant day-to-day variability in the rate of gastric emptying has been noted.

Due to a lack of standardization of the test and small sample sizes referenced in published studies, the capability of the gastric emptying test to discriminate between healthy individuals and those with known gastroparesis is uncertain. In a 2000 study by Tougas et al, 123 healthy subjects were assessed to determine the normal period required for nearly complete evacuation of a standardized meal from the stomach. The authors suggested that the threshold of normality for gastric retention at 4 hours is 10% meal retention. The cutoff point was set to include 95% of normal persons. However, it appears to be unknown if this same threshold identifies adequately 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). Studies that included only healthy participants were excluded from the review; rather, AHRQ looked for studies with comparison groups consisting of healthy, asymptomatic (i.e., 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 seven studies with diagnostic agreement ranging from 58% to 86% for test agreement when results were positive and 64% to 81% when test results were negative. There was moderate correlation between the ingestible capsule and gastric emptying scintigraphy on transit data and device agreement in five studies. Three studies that evaluated transit time reported similar sensitivity and specificity for the ingestible capsule and scintigraphy.

In 2008, Cassily et al evaluated the SmartPill and simultaneous gastric emptying scintigraphy in 15 healthy subjects. 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 0.606 and to 90% gastric emptying time was 0.565. The average amount of meal remaining in the stomach at the time the SmartPill exited the stomach was 5.4%. This study only shows 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 tests for gastroparesis were evaluated with both the SmartPill and gastric emptying scintigraphy. In this study, subjects ingested the capsule just before ingesting the standard meal. This resulted in five 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 two others dropped out.

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

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

A 2009 study by Maqbool et al assessed SmartPill and gastric emptying scintigraphy in ten healthy asymptomatic subjects. Emptying time assessed by SmartPill was correlated with the percent meal retained at two and four hours. The correlation between SmartPill and two hour scintigraphy was 0.95. The correlation between SmartPill and four-hour scintigraphy was 0.73.

A 2013 study by Green et al assessed SmartPill and gastric emptying scintigraphy in 22 pediatric patients with severe upper gastrointestinal symptoms. Of 20 evaluable patients who had both tests, nine patients had delayed gastric emptying identified by scintigraphy. SmartPill was 100% sensitive and 50% specific for delayed gastric emptying. Patients also underwent antroduodenal manometry (ADM) for detection of motor abnormalities. SmartPill identified motor abnormalities in 17 patients, compared with 10 detected by ADM. However, there does not appear to be a reference standard for motor abnormalities. Thus it cannot be determined whether

SmartPill is more sensitive or has a higher false-positive rate for detection of motor abnormalities.

Section Summary: Clinical Validity for Gastric Emptying

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 gold 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. Ideally, the relevant population of subjects should symptomatic or are under evaluation for the diagnosis of gastroparesis. Although there was moderate correlation between SmartPill gastric emptying time and scintigraphy, scintigraphy itself has limited reliability. Though the areas under the curve between the SmartPill and scintigraphy are similar, the modest correlation between the two tests indicates that there are often discordant results.

Colon Transit Time

Few studies evaluate the use of SmartPill for evaluating colonic transit times. In a 2013 systematic review by AHRQ, the strength of evidence in available studies on the ingestible capsule was found to be low overall. The 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 five studies with correlation coefficients ranging from 0.69 to 0.71.

In the 2009 study by Maqbool et al (referred to earlier), healthy asymptomatic individuals underwent simultaneous whole-gut scintigraphy and SmartPill assessment of whole gut transit times. The two techniques correlated with each other reasonably well. In a 2009 study by Rao et al, healthy subjects and subjects with constipation had whole gut transit times assessed with radio-opaque markers and the SmartPill. The diagnostic accuracy of the two techniques in differentiating the two groups of patients was similar. In 2010, Camilleri and colleagues compared the wireless motility capsule to radio-opaque markers in 158 patients with chronic functional constipation. In this multicenter validation study, the authors reported 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 – 0.98). No serious adverse events occurred in the study.

The FDA has received one 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: Clinical Validity for Colonic Transit Time

Although these studies show moderate correlations between SmartPill and other methods for assessing colonic transit times, they should be interpreted with caution. Two of the studies included healthy subjects, who are not the appropriate sample needed to evaluate 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

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 there was limited evidence available on the clinical impact of testing with the ingestible capsule. Therefore, the evidence was insufficient to draw conclusions regarding the impact of ingestible capsule testing results on treatment and management decisions.

In a 2011 retrospective study of 83 patients evaluated for gastroparesis, small intestinal dysmotility and slow transit constipation, Kuo and colleagues found wireless motility capsule testing resulted in a new diagnosis in 44 patients (53%). Clinical management changes were recommended in 65 patients. These included changes in medication regimens in 39 patients (60%) and in nutrition programs in nine 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 of 52 patients (17%), barium radiography testing in 7 of 13 patients (54%), and radio-opaque marker testing in 41 of 60 patients (68%). The authors noted a need for prospective studies to further understand wireless motility capsule testing and its role in patient management.

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

In a 2015 retrospective review of patients who underwent evaluation with SmartPill for suspected multiregional GI dysmotility, Arora et al found abnormal test results in 109/161 (67.7%) of subjects. Of these patients, multiregional dysmotility was diagnosed in 54 (49.5%) of patients. Although this study demonstrates a high yield of diagnosis among patients with a particular suspected condition, it does not demonstrate improved patient outcomes compared to standard tests.

Section Summary: Clinical Utility for Wireless Pressure Capsule

The evidence on the clinical utility of wireless pressure capsule is very limited, consisting of three retrospective analyses describing outcomes of patients undergoing testing with SmartPill.

These studies each lacked control subjects who are either diagnosed without the test or with alternative tests. 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.

Summary

For individuals who have suspected disorders of gastric emptying or slow-transit constipation who receive diagnostic testing with an ingestible pH and pressure capsule, the evidence includes studies of test characteristics and case series of patients who have undergone the test. Relevant outcomes are test accuracy and validity, other performance measures, symptoms, functional outcomes, and health status measures. Available studies provide some information regarding the comparison of SmartPill to other techniques for measuring gastric emptying and colonic transit times. This evidence primarily consists of concordance with available tests. Because the available tests, such as gastric emptying 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. It is not possible to determine whether there is net improvement in health using SmartPill versus standard diagnostic tests. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements

American Neurogastroenterology and Motility Society

The American Neurogastroenterology and Motility Society issued a consensus statement on intraluminal measurement of gastrointestinal and colonic motility in clinical practice in 2008. 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.

American and European Neurogastroenterology and Motility Societies

The American and European Neurogastroenterology and Motility Societies issued a position paper on gastrointestinal transit evaluation in 2011. 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.

American Gastroenterological Association

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

U.S. Preventive Services Task Force Recommendations
Not applicable

Key Words:
SmartPill®, GI monitoring system, ingestible pH and pressure capsule

Approved by Governing Bodies:
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. For example, an increase of two or more pH units usually indicates gastric emptying, and a subsequent decrease of one or more pH units usually indicates passage to the ileocecal junction. 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 GI 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.

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.

Benefit Application:
Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

Current Coding:
CPT Codes:

91112	Gastrointestinal transit and pressure measurement, stomach through colon, wireless capsule, with interpretation and report

References:

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Policy History:

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Medical Policy Group, December 2010
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