MEDICAL POLICY

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MEDICAL POLICY DETAILS	
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Product Disclaimer	• *If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.* • *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.* • *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.* • *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.*

POLICY STATEMENT

I. Based upon our criteria and assessment of the peer-reviewed literature, capsule endoscopy of the esophagus and small intestine (CPT 91110 & 91111) has been medically proven to be effective and, therefore, is considered **medically necessary** for **any** of the following indications:
   A. To investigate suspected small bowel bleeding (e.g., persistent or recurrent iron-deficiency anemia, positive fecal occult blood test, or visible bleeding) when conventional diagnostic workup failed to identify the source of bleeding.
   B. For the initial diagnosis of suspected Crohn's disease (CD) when conventional diagnostic work-up failed to reveal evidence of disease, and there remains a strong clinical suspicion of CD (e.g., chronic diarrhea, abdominal pain, weight loss, fatigue, fever, anemia, elevated white blood cell (WBC) count, and/or elevated laboratory markers of inflammation).
   C. For re-evaluation of members with an established diagnosis of Crohn's disease who remain symptomatic despite appropriate medical therapy.
   D. Surveillance of the small bowel in members with a diagnosis of hereditary polyposis syndromes (i.e., familial adenomatosis polyposis [FAP] or Peutz-Jeghers syndrome).
   E. Screening or surveillance of esophageal varices, in cirrhotic patients with significantly compromised liver function (i.e., Child-Pugh score of Class B or greater), where a standard upper endoscopy with sedation or anesthesia is contraindicated.
   F. For re-evaluation of members with an established diagnosis of celiac disease who remain symptomatic despite adherence to appropriate medical therapy.

II. Based upon our criteria and assessment of peer-reviewed literature, wireless capsule endoscopy has not been medically proven to be effective and, therefore, is considered **investigational** for any other indication, including but not limited to:
   A. Evaluating or diagnosing disease in the esophagus and/or small bowel, other than as stated above;
   B. Confirmation of lesions/pathology found by other diagnostic means;
   C. As the initial procedure in the diagnosis of GI bleeding, where upper endoscopy or colonoscopy has not been performed;
   D. For the diagnosis of irritable bowel syndrome;
   E. For the diagnosis of diseases of the stomach; or
   F. For the diagnosis of diseases of the large intestine/colon.

III. Based upon our criteria and assessment of the peer-reviewed literature, the following capsules have not been medically proven to be effective and, therefore, are considered **investigational** for **ALL** indications:
   A. Motility capsule endoscopy (e.g., SmartPill GI Monitoring System) (CPT 91112);
   B. Colon capsule endoscopy (e.g., PillCam COLON2) (CPT 91113);
   C. Patency capsule (e.g., Agile Patency Capsule or PillCam Patency Capsule) (CPT 91299);
   D. Magnetically controlled capsule endoscopy (e.g., NaviCam) (CPT 0651T).

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

POLICY GUIDELINES

I. Wireless CE must be performed under the supervision of a gastroenterologist with expertise in this technology and performed only when there is no suspected or confirmed GI obstruction.

II. In the case of suspected small bowel bleeding, because of low lesion detection rate, a small bowel follow-through or enteroclysis is not necessarily required prior to wireless CE. A small bowel follow-through may be beneficial in some cases, at the discretion of the clinician, prior to or after wireless CE, in the detection of small bowel lesions and in their anatomical localization.

DESCRIPTION

The small bowel is the most difficult portion of the bowel to examine. Because of its remoteness from the mouth and anus, and its relatively long length, conventional endoscopic techniques (gastroscopy, enteroscopy, and colonoscopy) are limited in their ability to provide a thorough examination of the small intestine. Conventional endoscopic techniques usually require intravenous sedation in an outpatient setting and can be uncomfortable for the patient.

According to the American College of Gastroenterology (ACG), bleeding from the small intestine is uncommon; however, with advances in small bowel imaging, the cause of bleeding in the small bowel can now be identified in most patients. Therefore, the term small bowel bleeding replaced the previous classification of obscure GI bleeding (OGIB). ACG recommends that the term OGIB be reserved for patients in whom a source of bleeding cannot be identified anywhere in the GI tract (Gerson et al., 2015).

Wireless Capsule Endoscopy (CE)

Wireless CE is a non-invasive diagnostic imaging device for use in the GI tract, especially the small bowel, which is not easily accessible to standard upper- and lower-endoscopic procedures. Examples of wireless CE devices include, but not limited to the PillCam SB or Capsule Endoscope System for small bowel use, PillCam ESO for esophageal use, and PillCam COLON2.

The wireless CE capsule, approximately the size of a vitamin, is swallowed by the patient, propelled by peristalsis through the gastrointestinal tract, and naturally excreted. As the capsule is propelled through the GI tract, the capsule records and transmits video images.

The capsule camera has been most frequently proposed as a technique to identify the source of suspected small bowel bleeding, where conventional diagnostic work-up has not provided a definitive diagnosis. Wireless CE has also been proposed as a diagnostic tool for other abnormalities of the GI tract (e.g., Crohn's disease) Capsule endoscopy may also

be useful for identifying celiac disease of the small intestine in persons with positive serologies where previous intestinal biopsies have been negative or when symptoms associated with celiac are refractory to standard medical therapy.

Patency Capsule

The patency capsule (e.g., Agile Patency System, Pillcam Patency Capsule) is a dissolvable capsule developed to verify adequate patency of the gastrointestinal tract prior to administration of the wireless CE in patients with known or suspected strictures. Once the patient ingests the patency capsule, it is propelled through the GI tract by normal peristalsis. If the patency capsule is excreted structurally whole, then this indicates patency of the patient's GI tract, and a PillCam capsule can be administered.

Wireless Motility Capsule

The wireless motility capsule is an alternative to gastric scintigraphy, which is considered the reference standard for diagnosing gastroparesis. The American Gastroenterological Association defines gastroparesis as delayed gastric emptying of the stomach, possibly due to issues with the stomach muscles, nerves, or brain and spinal cord nerves. Gastroparesis is not a mechanical block in the stomach. Symptoms of gastroparesis are often nonspecific and may mimic other gastrointestinal tract disorders. Gastroparesis can be caused by many conditions; most common causes include idiopathic, diabetic, or postsurgical.

The ingestible pH and pressure-sensing capsule (e.g., SmartPill GI Monitoring System) measures pH, pressure, and temperature changes of the GI tract, to evaluate gastric emptying for the diagnosis of gastroparesis, as well as colonic transit times. During wireless GI motility monitoring, the individual swallows a small capsule (approximately the size of a multivitamin) that contains sensors to measure peristaltic pressure, pH, and temperature. It assesses small bowel transit time by a sharp increase in pH on entry into the duodenum and by a fall in pH at the ileocecal junction. After excretion, the receiver is returned to the physician, who then downloads the data and analyzes the results.

Magnetic Capsule Endoscopy

Magnetically controlled capsule endoscopy, also referred to as magnetically assisted capsule endoscopy (MACE), is being investigated for visualization of the stomach and duodenum. This non-invasive system consists of a single-use ingestible capsule and magnet linked to a physician-operated console. The capsule contains a camera that wirelessly captures images of the desired anatomy. The console allows the operator to control the motion and direction of the capsule, ensuring visualization of the entire stomach. The capsule's camera captures images and transmits the images to a data recorder for interpretation. The procedure does not require sedation and has a procedural time of approximately 15 to 20 minutes. The capsule leaves the body in 24 hours on average but may take as long as 2 weeks. The device is contraindicated for use in patients with gastrointestinal obstruction, stenosis, fistula, or those with dysphagia. Other contraindications include patients with cardiac pacemakers or other implantable electronic medical devices as well as pregnant women, those less than 22 years of age, and those with a body mass index of 38 or greater.

RATIONALE

Wireless Capsule Endoscopy

The Given Diagnostic Imaging System, PillCam SB, received initial Section 510(k) marketing clearance from the FDA on August 1, 2001. The FDA cleared the device for use along with, not as a replacement for, other endoscopic and radiologic evaluations of the small bowel. On July 2, 2003, the FDA approved the PillCam SB as a first-line tool in the detection of abnormalities of the small bowel, removing the adjunctive tool qualifier. On October 29, 2003, the FDA announced that it had expanded its approved indications for the use of wireless CE, PillCam SB, to include visualization of the small bowel and detection of abnormalities in symptomatic children aged 10 to 18 years. This approval was based on data from a small trial where the wireless CE was able to diagnose or definitively exclude a bleeding source, small bowel polyps or Crohn's disease in 29 out of 30 children. In September 2009, the FDA expanded its approval of the PillCam SB for use in children aged two years and up.

The Olympus Capsule Endoscope System received Section 510(k) marketing clearance from the FDA in September 2007, as equivalent in intended use, method of operation, material, and design to the predicate device (PillCam SB). It is used for visualization of the small intestine mucosa. FDA approval was based upon a study of 51 patients with OGIB who

swallowed both the PillCam SB and the Endocapsule, 40 minutes apart and in randomized order. The devices were similar, in terms of the detection of normal versus abnormal small intestine mucosa and in their diagnostic capability (Cave et al. 2008).

There are very limited studies of wireless CE as a diagnostic tool for other diseases of the small bowel (e.g., carcinoma, celiac sprue), and they have yet to provide sufficient data on the diagnostic yield and changes in patient management.

Small bowel capsule endoscopy (SBCE) can be used as a surveillance tool for small bowel polyps in patients with inherited polyposis syndromes. SBCE has been found to have a better diagnostic capability to reveal small bowel polyps, compared to barium follow-through, in patients with Peutz-Jeghers syndrome (Brown 2006, Iaquinto 2008).

The PillCam ESO (Given Imaging) was approved by the FDA in November 2004 as a non-invasive alternative to endoscopy, to diagnose and evaluate diseases of the esophagus. Direct imaging of the small bowel with an endoscope is limited, and, thus, wireless CE of the small bowel occupies a unique diagnostic niche. In contrast, esophageal endoscopy, which also offers the opportunity for biopsy, is a routinely performed procedure. Therefore, assessment of CE of the esophagus requires comparison of its diagnostic performance to the gold standard of conventional endoscopy. One proposed indication for the capsule camera is detection of Barrett's esophagus, considered a premalignant condition associated with gastroesophageal reflux disease (GERD). Conventional endoscopy is often recommended in patients with longstanding symptoms of GERD, or in those requiring pharmacologic therapy to control GERD symptoms, to rule out Barrett's esophagus. This is a high-volume indication for conventional upper endoscopy, given the high prevalence of GERD.

Capsule endoscopy offers a potential alternative to endoscopy; patients with a negative study could potentially forego conventional endoscopy. In this setting, the negative predictive value of CE is the key diagnostic parameter. Patients who are believed to have suggestive findings of Barrett's esophagus will require a confirmatory conventional endoscopy with biopsy.

Eliakim et al. 2004 reported on an initial case series of 17 patients with suspected esophageal disorders. The negative predictive value for any esophageal disorder was 100%, while the positive predictive value was 92% (sensitivity 100%, specificity 80%). In a larger, multi-center study of 106 patients with either GERD or Barrett's esophagus, Eliakim et al. 2005 reported esophageal abnormalities in 66/106 patients, providing a sensitivity of 92% and specificity of 95%. In an abstract presentation at the 2004 Gastrointestinal Cancers Symposium of ASCO, Schnoll-Sussman et al. reported on the results of 53 consecutive patients who underwent both conventional and capsule camera endoscopy as part of an evaluation for Barrett's esophagus. The sensitivity of the capsule camera in detecting Barrett-like changes was 67%, while the specificity was 75%. The positive predictive value was 35%, and the negative predictive value was 92%. The results of these relatively small studies are inadequate to permit scientific conclusions regarding the clinical role of esophageal CE. Studies (n = 73) have been published, comparing the Pill Cam ESO to upper endoscopy in patients with portal hypertension and esophageal varices (Eisen et al. 2006; Lapalus et al. 2006, and Penna et al. 2008). Based on the outcomes of these small studies, PillCam ESO may represent an accurate, non-invasive alternative to EGD for the detection of esophageal varices and portal hypertensive gastropathy. While further studies are required to validate these initial findings, the use of wireless CE for those patients with significantly compromised liver function, who cannot tolerate sedation or anesthesia, appears reasonable.

A tethered or string CE for esophageal use remains under investigation. Strings and a sling are attached to the CE to allow for multiple controlled passes across the esophagus, with the aim of improving transit time. The ability to completely retrieve the device eliminates the risk of capsule retention in susceptible patients and also offers an advantage over conventional wireless CE. A preliminary study of 40 patients with dysphagia (Gilani et al. 2007) found that tethered CE was safe and well-tolerated by patients. The overall agreement between tethered CE and traditional upper endoscopy was 92.7%. Larger studies are needed, to determine its efficacy/accuracy and to further define its role as an alternative to upper endoscopy.

The American College of Gastroenterology's guideline for the diagnosis and management of celiac disease does not address capsule endoscopy (Rubio-Tapia et al., 2023). However, The American Gastroenterological Association's (AGA) Clinical Practice Guideline on the Management of Refractory Celiac Disease issued a best practice statement that supports performing small bowel imaging with capsule endoscopy and computed tomography or magnetic resonance enterography to exclude enteropathy-associated T-cell lymphoma and ulcerative jejunoileitis at initial diagnosis of type 2 refractory

celiac disease (RCD2) (Green et al., 2022). Capsule endoscopy can help quantify the extent and severity of villous atrophy, as well as look for these complications. CT or MR enterography are complementary to capsule endoscopy, and may show findings such as bowel wall thickening, mesenteric adenopathy, small bowel masses, or ulcerative jejunoileitis.

The AGA's best practice advice also indicates that repeat imaging should be obtained in patients with RCD2 who are clinically worsening due to the increased risk of lymphoma. The presence of strictures, inflammation, erosions, ulcers, or mass lesions on capsule endoscopy or cross-sectional imaging should prompt further evaluation with small bowel enteroscopy to secure a pathologic diagnosis.

According to Turner et al. (2021), the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) initiative began in 2015 when the International Organization for the Study of Inflammatory Bowel Diseases (IOIBD) published proposed treatment targets for adult patients with inflammatory bowel disease (IBD). This survey identified the following targets as most important: clinical response and remission, endoscopic healing, and normalization of C-reactive protein/erythrocyte sedimentation rate and calprotectin. An updated STRIDE-II was published in 2021, confirming STRIDE-I's long-term targets of clinical remission and endoscopic healing and added absence of disability, restoration of quality of life, and normal growth in children.

STRIDE-II encompasses evidence- and consensus-based recommendations for treat-to-target strategies in adults and children with IBD. Consensus statement number eight recommends endoscopic and transmural assessment of healing by sigmoidoscopy or colonoscopy; however, when not feasible, alternatives can be capsule endoscopy or balloon enteroscopy. Although the authors acknowledge that transmural healing in Crohn's disease is becoming an important adjuvant assessment of the depth of treatment response, STRIDE-II states that more research is needed to determine the incremental gain derived from the goal and whether the gain is worth the therapy-related risks and costs.

Colon Capsule Endoscopy

Given Imaging received FDA Section 510(k) clearance (Class II) for the PillCam COLON 2 in February 2014. The clearance is intended for use in patients who had an incomplete traditional colonoscopy and still require a better review of the passageway. Given Imaging conducted an 884-patient, 16-site clinical trial that studied the accuracy and safety of PillCam COLON 2, compared to optical colonoscopy, in detecting adenomas 6 millimeters or larger. Results from this clinical trial demonstrated that the sensitivity for PillCam COLON was 88% and specificity was 82% in detecting adenomas at least 6 mm in size. The FDA based its clearance decision on an analysis of this clinical trial data, which used a more restrictive methodology for matching polyps. In this analysis, which was conducted on hyperplastic polyps and adenomas, the positive percent agreement for PillCam COLON and optical colonoscopy was 69%, and negative percent agreement was 81% for polyps at least 6 millimeters in size. The wireless capsule had not been adequately studied in the large intestine. The colon was not well-visualized due to stool obscuring the colonic mucosa. Adequate visualization of the colon was also hampered by the colon's larger diameter which made it possible for the capsule camera to miss suspicious areas. R Eliakim et al. (2006) conducted a prospective study to determine whether CE of the colon can provide similar detection rates of pathological colonic conditions, compared to conventional colonoscopy. Conventional colonoscopy detected more polyps compared to wireless CE: 70% were identified with the capsule and 16/20 (80%) were identified by conventional colonoscopy. In comparison with conventional colonoscopy, false-positive findings on PillCam Colon capsule examination were recorded in 15/45 cases (33%). Additional studies are needed, to evaluate the accuracy of PillCam Colon endoscopy in patient populations with different prevalence levels of colonic disease. A prospective study by Parodi et al. (2018) included 177 first-degree relatives of individuals with colorectal cancer and found, for lesions 6 mm or larger, a sensitivity of 91% (95% CI, 81% to 96%) and specificity of 88% (95% CI, 81% to 93%) for colon CE, using optical colonoscopy as the reference.

For individuals who are screened for colon cancer who receive wireless CE, the evidence includes diagnostic accuracy studies and systematic reviews. No RCTs assessing the clinical utility of wireless CE were identified.

Studies of CE in screening populations are necessary to determine the diagnostic characteristics of the test in this setting. Studies of diagnostic characteristics alone are insufficient evidence to determine the efficacy of CE for colon cancer screening. Because diagnostic performance is worse than standard colonoscopy, CE would need to be performed more frequently than standard colonoscopy to have comparable efficacy.

Cash et al (2021) evaluated the diagnostic characteristics of CE using subsequently performed colonoscopy as the reference standard. Randomizing patients to colon CE or computed tomography (CT) colonography followed by optical colonoscopy. Data from 286 patients revealed that the proportion of enrollees with any polyp 6 mm or larger confirmed by subsequent blinded optical colonoscopy was 31.6% for colon CE versus 8.6% for CT colonography. The sensitivity and specificity of colon CE for polyps 6 mm or larger was 79.2% and 96.3%, respectively, while that of CT colonography was 26.8% and 98.9%. For polyps 10 mm or larger, the sensitivity and specificity of colon CE was 85.7% and 98.2% compared with 50% and 99.1% for CT colonography. The authors concluded that colon CE should be considered comparable or superior to CT colonography as a screening test; however, neither test was as effective as optical colonoscopy.

Kjolhede et al (2020) reported on a systematic review and meta-analysis of the diagnostic accuracy of CE compared to colonoscopy with stratified results for polyps of any size, polyps ≥ 6 mm, and polyps ≥ 10 mm. Across analyzed patients in the 12 eligible studies, the indications for endoscopy included colorectal cancer screening or history of polyps or colorectal cancer (n=1200 [63.2%]), positive fecal immunochemical test (n=493 [26%]), first-degree relatives of patients with colorectal cancer (n=177 [9.3%]), or unspecified (n=28 [1.5%]). The rate of patients with an adequate bowel preparation ranged from 40% to 100%. The rates of complete CE transits ranged from 57% to 100%. The authors note that the relatively high rate of incomplete CE investigations limits the utility of CE in the colorectal cancer setting. All but 1 study was assessed to have a high risk of bias and applicability concerns for the reference standard.

The American College of Gastroenterology clinical guidelines for colorectal cancer screening (Shaukat et al., 2021) suggest consideration of the colon capsule for screening [conditional recommendation; very low quality].

Without direct evidence of efficacy in a clinical trial of colon cancer screening using CE, modeling studies using established mathematical models of colon precursor incidence and progression to cancer could provide estimates of efficacy in preventing colon cancer mortality. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Patency Capsule

The FDA approved the Agile patency capsule in May 2006 as “an accessory to the Pill Cam video capsule,” noting that it “is intended to verify adequate patency of the gastrointestinal tract prior to administration of the Pill Cam video capsule in patients with known or suspected strictures.” Delvaux et al. (2005) evaluated the usefulness of this system in 22 patients with suspected intestinal stenosis who were also undergoing CE. The authors stated that the current technical development of the patency capsule limits its use in clinical practice, as it did not detect stenoses undiagnosed by computed tomography (CT) or small bowel follow-through. They also stated that the start of dissolution at 40 hours after ingestion was too slow to prevent episodes of intestinal occlusion. The authors noted that patients with Crohn's disease are most likely to be at risk of blockage of progression of the capsule and should benefit from a CT investigation before CE. They noted that a careful interview eliciting the patient's medical history and symptoms remains the most useful indicator with regard to suspicion of an intestinal stenosis. Signorelli et al. (2006) evaluated 32 patients. The 26 patients who excreted the patency capsule intact, without experiencing abdominal pain, were deemed eligible for the CE procedure, which was performed uneventfully in the 25 who agreed to undergo the examination. The authors stated that the patency capsule “is an effective method for the assessment of small bowel patency before CE. However, the real incidence of complications such as the development of severe abdominal pain and small bowel obstruction needs to be ascertained before the patency test can be recommended as the standard method to evaluate patients at risk of developing capsule retention.” There is a lack of data defining the safety and role of the patency capsule. Conventional evaluations remain the gold standard for ruling out any known or suspected gastrointestinal obstruction, strictures, and fistulas, prior to CE.

Wireless Motility Capsule

In 2006, the ingestible capsule (SmartPill GI Monitoring System) was FDA-cleared through the Section 510(k) process for the evaluation of 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 means passage to the ileocecal junction. The capsule also measures pressure and temperature during its transit through the entire GI tract, allowing calculations of total GI tract 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 and normal transit constipation. The SmartPill is not for use in pediatric patients.

The American Gastroenterological Association's 2013 guidelines on gastroparesis diagnosis and treatment indicated that WCE testing requires validation before it can be considered as an alternative to scintigraphy for diagnosing gastroparesis. There is a lack of data defining the safety and role of the SmartPill. Standard tests used in the evaluation of constipation include ingestion of radiopaque markers and colonic transit scintigraphy.

In a systematic review by Stein et al. (2013) that was conducted for the Agency for Healthcare Research and Quality (AHRQ), the strength of evidence in available studies on the ingestible capsule for assessing colonic transit times was found to be low overall. No studies were identified that compared the SmartPill to colonic scintigraphy. Accuracy of the ingestible capsule in diagnosing slow-transit constipation was similar to tests using radiopaque markers. A moderate correlation between colonic transit times with the ingestible capsule and tests with radiopaque markers was shown in five studies (range, 0.69-0.71). The overall strength of evidence favoring the ingestible capsule was low. There was a moderate correlation on transit data and device agreement between the ingestible capsule and gastric emptying scintigraphy in five studies.

The American College of Gastroenterology's clinical guideline on "Management of gastroparesis" (Camilleri et al. 2013) noted, "Alternative approaches for assessment of gastric emptying include wireless capsule motility testing and 13C breath testing using octanoate or spirulina incorporated into a solid meal; they require further validation before they can be considered as alternates to scintigraphy for the diagnosis of gastroparesis" (conditional recommendation, moderate level of evidence).

Surjanhata et al. (2018) performed a retrospective, multi-center clinical trial of 190 participants, to evaluate colonic wake response using the WMC. Colonic wake response is a relative increase in colonic motility upon awakening as colonic manometry studies have demonstrated reduced wake response in slow transit subjects. WMC motility parameters of contraction frequency (Ct) and area under the contraction curve (AUC) were analyzed in 20-minute windows one hour before and after awakening for all study participants. The participants were evaluated at the study center at 48 hours post ingestion and then returned the data receiver and diary at 120 hours post ingestion. Recorded WMC events were correlated with the participants' diary entries and pH tracings to quantify transit times of gastric emptying, small bowel transit, and colonic transit. At baseline prior to awakening, there was no significant difference in the mean contraction frequency (Ct) between the study participants ($p > 0.15$). At 20, 40, and 60 minutes after awakening, e4 (STC) subjects had significantly lower mean Ct when compared to H ($p < 0.001$) and NTC ($p < 0.01$). Linear regression demonstrated that outlet obstruction was not associated with a decreased wake response ($\beta = 3.94$, (CI −3.12–1.00), $P = 0.27$). Blunted wake response sensitivity was 84% and specificity was 32% for chronic constipation at the Ct threshold of 64 at 20-min post-wake. The authors concluded that WMC technology can be utilized to identify an impaired wake response in subjects with STC and not normal transit constipation (NTC) which may support previous studies of neuronal dysfunction as an etiology of STC and potential for pharmacologic intervention.

Two large, prospective, multicenter trials (Lee et al., 2019 and Hasler et al., 2019) compared WMC testing with gastric emptying scintigraphy (GES) in patients with gastroparesis symptoms. Both studies found that WMC detected delayed gastric emptying more often than GES, due to WMC's capability of profiling the entire gastrointestinal tract in patients. However, the studies were limited by practice standards, participant population, and lack of correlation of physiological results with symptoms and/or management outcomes. Additional clinical studies are needed, to further investigate and compare GES versus WMC testing in patients with gastroparesis symptoms. One small prospective, single center, cohort study (Sangnes et al.,2020) compared WMC with scintigraphy in individuals with diabetic gastroparesis, with the objective of assessing diagnostic reliability. Although the researchers reportedly found a strong correlation between WMC and 4-hour GES, the study was limited by its small study size ($n = 66$) and a patient cohort that may have been more severely affected by their disease.

The available published evidence demonstrates that the diagnostic accuracy of the SmartPill is not well-defined. The current reference standard, gastric emptying scintigraphy, is an imperfect standard, which creates difficulty in defining the sensitivity and specificity of the SmartPill. There is moderate correlation between the SmartPill and scintigraphy. For constipation, studies showed moderate correlation between the SmartPill and other methods of assessing colonic transit times and should be interpreted cautiously.

Magnetic Capsule Endoscopy (CE)

The FDA approved a novel magnetically maneuvered CE system (NaviCam; AnX Robotica, Inc.) in May 2020.

For individuals who have unexplained upper abdominal complaints who receive magnetic CE, the evidence includes diagnostic accuracy studies. Studies evaluating the diagnostic characteristics of magnetic CE as compared to conventional gastroscopy in the target population have generally demonstrated similar accuracy, sensitivity, and specificity, with increases in patient preference and an acceptable safety profile with the magnetic CE approach. However, the diagnostic characteristics of magnetic CE are inadequate to substitute for other modalities or to triage patients to other modalities based on the current literature. Direct evidence of improved outcomes or a strong chain of evidence to improved outcomes is lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).*

CPT Codes

Code	Description
91110	Gastrointestinal tract imaging, intraluminal (e.g., capsule endoscopy), esophagus through ileum, with interpretation and report
91111	Gastrointestinal tract imaging, intraluminal (e.g., capsule endoscopy), esophagus with interpretation and report
91112 **(E/I)**	Gastrointestinal transit and pressure measurement, stomach through colon, wireless capsule, with interpretation and report
91113 **(E/I)**	Gastrointestinal tract imaging, intraluminal colon
91299 **(*E/I)**	Unlisted diagnostic gastroenterology procedure *(*E/I when billed as use of patency capsule)*
0651T **(E/I)**	Magnetically controlled capsule endoscopy, esophagus through stomach, including intraprocedural positioning of capsule, with interpretation and report.

HCPCS Codes

Code	Description
No codes	

ICD10 Codes

Code	Description
Multiple codes	

REFERENCES

*ASGE Standards of Practice Committee, et al. Guideline: The role of endoscopy in inflammatory bowel disease. Gastrointestinal Endoscopy 2015 May 22;81(5):1101-1121.E13. [doi.org/10.1016/j.gie.2014.10.030] accessed 05/31/23.

*ASGE Standards of Practice Committee, et al. Guideline: The role of endoscopy in the management of suspected small-bowel bleeding. Gastrointestinal Endoscopy 2017 Jan;85(1):22-31. [doi.org/10.1016/j.gie.2016.06.013] accessed 05/31/23.

ASGE Training Committee, et al. Technology status evaluation report: video capsule endoscopy. Gastrointestinal Endoscopy 2021 Apr;93(4):784-796. [doi.org/10.1016/j.gie.2020.12.001] accessed 05/31/23.

*Albert JG, et al. Impact of capsule endoscopy on outcome in mid-intestinal bleeding: a multicentre cohort study in 285 patients. Eur J Gastroenterol Hepatol 2008 Oct;20(10):971-7.

*Amano Y, et al. Gastric screening examination using PillCam ESO 2: a pilot study. Dig Liver Dis 2011 Jul;43(7):580-1.

Baltes P, et al. PillCamColon2 after incomplete colonoscopy - a prospective multicenter study. World J Gastroenterol 2018 Aug 21;24(31):3556-3566.

*Banerjee R, et al. Safety and efficacy of the M2A patency capsule for diagnosis of critical intestinal patency: results of a prospective trial. J Gastroenterol Hepatol 2007 Dec;22(12):2060-63.

*Barret M et al. Diagnostic yield of capsule endoscopy in refractory celiac disease. Am J Gastroenterol 2012;107:1546-1553.

Boland RC, et al. Clinical practice guidelines. Diagnosis and management of cancer risk in the gastrointestinal hamartomatous polyposis syndromes: recommendations from the US multi-society task force (USMSTF) on colorectal cancer. Gastroenterol 2022;162:2063-2085.

*Bhardwaj A, et al. A meta-analysis of the diagnostic accuracy of esophageal capsule endoscopy for Barrett's esophagus in patients with gastroesophageal reflux disease. Am J Gastroenterol 2009 Jun;104(6):1533-9.

*Bourreille A, et al. Role of small-bowel endoscopy in the management of patients with inflammatory bowel disease: an international OMED-ECCO consensus. Endoscopy 2009;41:618-37.

Brito HP, et al. Video capsule endoscopy vs double-balloon enteroscopy in the diagnosis of small bowel bleeding: a systematic review and meta-analysis. World J Gastrointest Endosc 2018 Dec 16;10(12):400-421.

Bruining DH, et al. BLINK study group. Panenteric capsule endoscopy versus ileocolonoscopy plus magnetic resonance enterography in Crohn's disease: a multicentre, prospective study. BMJ Open Gastroenterol 2020 Jun;7(1):e000365.

*Camilleri M, et al. Clinical guideline: management of gastroparesis. Am J Gastroenterol 2013 Jan;108(1):18–38.

*Casciani E, et al. MR enterography versus capsule endoscopy in paediatric patients with suspected Crohn's disease. Eur Radiol 2011 Apr;21(4):823-31.

Cash BD, et al. Multicentre, prospective, randomised study comparing the diagnostic yield of colon capsule endoscopy versus CT colonography in a screening population (the TOPAZ study). Gut 2021;70(11):2115-2122.

*Cave D, et al. A Multicenter randomized comparison of the endocapsule and the PillCam SB. Gastrointest Endosc 2008; Sep;68(3):487-94.

*De Franchis R, et al. Esophageal capsule endoscopy (PillCam ESO) is comparable to traditional endoscopy for detection of esophageal varices- an international multicenter trial. Gastrointest Endosc 2007;65(5):AB107.

*Delvaux M, et al. Esophageal capsule endoscopy in patients with suspected esophageal disease: double blinded comparison with esophagogastroduodenoscopy and assessment of interobserver variability. Endoscopy 2008 Jan;40(1):16-22.

*Dionisio PM, et al. Capsule endoscopy has a significant higher diagnostic yield in patients with suspected and established small-bowel Crohn's disease: a met-analysis. Am J Gastroenterol 2010 Jun;105(6):1240-8.

*Eliakim R, et al. Evaluation of the Pill Cam Colon capsule in the detection of colonic pathology: results of the first multicenter, prospective, comparative study. Endoscopy 2006 Oct;38(10):963-70.

*Eliakim R, et al. Prospective multicenter performance evaluation of the second-generation colon capsule compared with colonoscopy. Endoscopy 2009 Dec;41(12):1026-31.

*El-Matary W, et al. Diagnostic characteristics of given video capsule endoscopy in diagnosis of celiac disease: A meta-analysis. J Laparoendosc Adv Surg Tech A 2009 Apr 30 [Epub ahead of print].

Ferretti F, et al. Effectiveness of capsule endoscopy and double-balloon enteroscopy in suspected complicated celiac disease. Clin Gastroenterol Hepatol 2020;20:941-949.

Food and Drug Administration. PillCam® COLON 2 Capsule Endoscopy System. [http://www.accessdata.fda.gov/cdrh_docs/pdf12/K123666.pdf] accessed 07/20/23.

*Fritscher-Ravens A, et al. The feasibility of wireless capsule endoscopy in detecting small intestinal pathology in children under the age of 8 years: a multicentre European study. Gut 2009 Nov;58(11):1467-72.

*Galmiche JP, et al. Screening for esophagitis and Barrett's esophagus with wireless esophageal capsule endoscopy: a multicenter prospective trial in patients with reflux symptoms. Am J Gastroenterol 2008 Mar;103(3):538-45.

*Gerson LB, et al. ACG clinical guideline: Diagnosis and Management of Small Bowel Bleeding. Am J Gastroenterol 2015 Sep;110(9):1265-1287.

*Green PHR, et al. AGA clinical practice update on management of refractory celiac disease: expert review. Gastroenterol 2022 Nov;163(5):1461-1469.

González-Suárez B, et al. Colon capsule endoscopy versus CT colonography in FIT-positive colorectal cancer screening subjects: a prospective randomised trial-the VICOCA study. BMC Med 2020 Sep 18;18(1):255.

*Gostout C. Capsule endoscopy clinical update: American Society for Gastrointestinal Endoscopy. 2002 Oct;10(2):1-4.

*Gupta A, et al. A prospective study of MT enterography versus capsule endoscopy for the surveillance of adult patients with Peutz-Jeghers syndrome. AJR Am J Roentgenol 2010 Jul;195(1):108-16.

*Guturu P, et al. Capsule endoscopy with PillCAM ESO for detecting esophageal varices: a meta-analysis. Minerva Gastroenterol Dietol 2011 Mar;57(1):1-11.

*Hartmann D, et al. A prospective two-center study comparing wireless capsule endoscopy with intraoperative enteroscopy in patients with obscure GI bleeding. Gastrointest Endosc Jun 2005;61(7):826-832.

*Hasler WL, et al. Influence of gastric emptying and gut transit testing on clinical management decisions in suspected gastroparesis. Clinical and Translational Gastroenterology 2019;10:e00084.

Kjolhede T, et al. Diagnostic accuracy of capsule endoscopy compared with colonoscopy for polyp detection: systematic review and meta-analyses. Endoscopy 2021 Jul;53(7):713-721. PMID 32858753.

Kim ER. Roles of Capsule Endoscopy and Device-Assisted Enteroscopy in the Diagnosis and Treatment of Small-Bowel Tumors. Clin Endosc 2020;53:410-416.

*Lai LH, et al. Long-term follow-up of patients with obscure gastrointestinal bleeding after negative capsule endoscopy. Am J Gastroenterol 2006 Jun;101(6):1224-8.

*Laine L, et al. Does capsule endoscopy improve outcomes in obscure gastrointestinal bleeding? Randomized trial versus dedicated small bowel radiography. Gastroenterol 2010 May;138(5):1673-80.

*Lee AA, et al. Validation of diagnostic and performance characteristics of the wireless motility capsule in patients with suspected gastroparesis. Clinical Gastroenterology and Hepatology 2019;17:1770–1779.

*Leighton J, et al. Quality indicators for capsule endoscopy and deep enteroscopy. Am J of Gastroent 2022 Nov;117(11):1780-1796.

Lichtenstein GR, et al. ACG clinical guidelines. Management of Crohn's disease in adults. Am J Gastroenterol 2018 Mar; 113:481–517 [doi: 10.1038/ajg.2018.27]. accessed 05/30/23.

*Lin OS, et al. Blinded comparison of esophageal capsule endoscopy versus conventional endoscopy for a diagnosis of Barrett's esophagus in patients with chronic gastroesophageal reflux. Gastrointest Endosc 2007 Apr;65(4):577-83.

*Long MD, et al. Impact of capsule endoscopy on management of inflammatory bowel disease: a single tertiary care center experience. Inflamm Bowel Dis 2011 Sep;17(9):1855-62.

*Lu Y, et al. Meta-analysis of capsule endoscopy in patients diagnosed or suspected with esophageal varices. World J Gastroenterol 2009 Mar 14;15(10):1254-8.

*Marmo R, et al. Capsule endoscopy versus enteroclysis in the detection of small-bowel involvement in Crohn's disease: a prospective trial. Clin Gastroenterol Hepatol 2005 Aug;3(8):772-6.

Marya NB, et al. A randomized controlled trial comparing efficacy of early video capsule endoscopy with standard of care in the approach to non-hematemesis gastrointestinal bleeding (with videos). Gastrointest Endosc 2019 Jan;89(1):33-43.e4.

*Mergener K, et al. Literature review and recommendations for clinical application of small-bowel capsule endoscopy, based on a panel discussion by international experts. Consensus statements for small-bowel capsule endoscopy, 2006/2007. Endoscopy 2007 Oct;39(10):895-909.

*Milano A, et al. A prospective evaluation of iron deficiency anemia in the GI endoscopy setting: role of standard endoscopy, videocapsule endoscopy, and CT-enteroclysis. Gastrointest Endosc 2011 May;73(5):1002-8.

*National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology v1.2023 – May 17, 2023. Colorectal Cancer Screening. [https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf] accessed 07/11/23.

Nemeth A, et al. Video capsule endoscopy in pediatric patients with Crohn's disease: a single-center experience of 180 procedures. Therap Adv Gastroenterol 2018 Mar 4;11:1756284818758929.

*Parodi A, et al. Colon capsule endoscopy to screen for colorectal neoplasia in those with family histories of colorectal cancer. Gastrointest Endosc 2018 Mar;87(3):695-704.

Pennazio M, et al., Small-bowel capsule endoscopy and device-assisted endoscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) guideline – update 2022. Endoscopy 2023 Jan;55(1):58-95. Epub 2022 Nov 24. PMID: 36423618.

*Postgate A, et al. Feasibility of video capsule endoscopy in the management of children with Peutz-Jeghers syndrome: a blinded comparison with barium enterography for the detection of small bowel polyps. J Pediatr Gastreoenterol Nutr 2009 Oct;49(4):417-23.

*Raju GS, et al. American Gastroenterological Association (AGA) Institute technical review on obscure gastrointestinal bleeding. Gastroenterol 2007 Nov;133(5):1697-717.

*Rubio-Tapia A, et al. American College of Gastroenterology guidelines update: diagnosis and management of celiac disease. Am J of Gastroenterol 2023 Jan;118(1):59-76.

*Rokkas T, et al. A meta-analysis evaluating the accuracy of colon capsule endoscopy in detecting colon polyps. Gastrointest Endosc 2010 Apr;71(4):792-8.

Sangnes DA, et al. Wireless motility capsule compared with scintigraphy in the assessment of diabetic gastroparesis. Neurogastroenterol & Motility 2020 Apr;32(4)e13771.

*Sharma P, et al. The diagnostic accuracy of esophageal capsule endoscopy in patients with gastroesophageal reflux disease and Barrett's esophagus: a blinded, prospective study. Am J Gastroenterol 2008 Mar;103(3):525-32.

Shahaeen NJ, et al. Diagnosis and management of barrett's esophagus: an updated ACG guideline. Am J Gastroenterol 2022;117:559-587.

Shaukat A, et al. ACG clinical guidelines: colorectal cancer screening 2021. Am J Gastroenterol 2021 Mar 01; 116(3): 458-479. [PMID 33657038]

Singh K, et al. Diagnostic yield of capsule endoscopy for small bowel arteriovenous malformations in patients with hereditary hemorrhagic telangiectasia: a systematic review and meta-analysis. Endosc Int Open 2019 Feb;7(2):E282-E289.

*Stein E, et al. Wireless motililty capsule versus other diagnostic technologies for evaluating gastroparesis and constipation: A comparative effectiveness review. 2013 May; AHRQ Publication No. 13-EHC060-EF.

*Surjanhata B, et al. Colonic motor response to wakening is blunted in slow transit constipation as detected by wireless motility capsule. Clinical and Translational Gastroenterology 2018 9:144.

Turner D, Riccuito A, Lewis A, D'Amico F, Dhaliwal J, et al. STRIDE-II: An update on the selecting therapeutic targets in inflammatory bowel disease (STRIDE) initiative of the international organization for the study of IBD (IOIBD): Determining therapeutic goals for treat-to-target strategies in IBD. Gastroenterol 2021 April:160(5):1570-1583.

Valdivia PC et al. Indications, detection, completion and retention rates of capsule endoscopy in two decades of use: a systematic review and meta-analysis. Diagnostics 2022 Apr;12(5)1105.

*Van Gossum A, et al. Capsule endoscopy versus colonoscopy for the detection of polyps and cancer. NEJM 2009 Jul 16;361(3):264-70.

Vuik FER, et al. Applicability of colon capsule endoscopy as pan-endoscopy: from bowel preparation, transit, and rating times to completion rate and patient acceptance. Endosc Int Open 2021;9:E1852-E1859.

Vuik FER, et al. Colon capsule endoscopy in colorectal cancer screening: a systematic review. Endoscopy 2021;53(8):815-824.

Yang et al, American Society for Gastrointestinal Endoscopy guideline on the role of endoscopy in familial adenomatous polyposis syndromes. Gastrointestin Endosc 2020;90:963982.e2.

Zammit SC & Sidhu R. Capsule endoscopy – Recent developments and future directions. Expert Review of Gastroenterology & Hepatology 2021 Vol 15;2: 127-137.

Zammitt SC et al. Small bowel capsule endoscopy in refractory celiac disease: a luxury or a necessity? Ann Gastroenterol 2021;34(2):188-195.

*Key Article

KEY WORDS

AGILE patency capsule, Capsule Endoscope System, Given capsule camera, PillCam SB, PillCam ESO, PillCam Colon, SmartPill, Treat-to-target.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

Based on our review, wireless capsule endoscopy and wireless motility capsule are not addressed in a Medicare National Coverage Determinations (NCD).

There is currently a Local Coverage Determination (LCD) for Colon Capsule Endoscopy (L38571). Please refer to the following LCD website for Medicare Members: [http://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=38571&ver=8&lcdStatus=all&sortBy=title&bc=6] accessed 05/30/23.