

# Local Coverage Determination (LCD): Helicobacter Pylori Infection Testing (L37626)

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## Contractor Information

| CONTRACTOR NAME                    | CONTRACT TYPE | CONTRACT NUMBER | JURISDICTION | STATE(S)     |
|------------------------------------|---------------|-----------------|--------------|--------------|
| Noridian Healthcare Solutions, LLC | A and B MAC   | 02101 - MAC A   | J - F        | Alaska       |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 02102 - MAC B   | J - F        | Alaska       |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 02201 - MAC A   | J - F        | Idaho        |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 02202 - MAC B   | J - F        | Idaho        |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 02301 - MAC A   | J - F        | Oregon       |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 02302 - MAC B   | J - F        | Oregon       |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 02401 - MAC A   | J - F        | Washington   |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 02402 - MAC B   | J - F        | Washington   |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03101 - MAC A   | J - F        | Arizona      |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03102 - MAC B   | J - F        | Arizona      |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03201 - MAC A   | J - F        | Montana      |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03202 - MAC B   | J - F        | Montana      |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03301 - MAC A   | J - F        | North Dakota |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03302 - MAC B   | J - F        | North Dakota |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03401 - MAC A   | J - F        | South Dakota |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03402 - MAC B   | J - F        | South Dakota |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03501 - MAC A   | J - F        | Utah         |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03502 - MAC B   | J - F        | Utah         |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03601 - MAC A   | J - F        | Wyoming      |
| Noridian Healthcare Solutions, LLC | A and B MAC   | 03602 - MAC B   | J - F        | Wyoming      |

## LCD Information

### Document Information

**LCD ID**

L37626

**Original Effective Date**

For services performed on or after 05/27/2019

**LCD Title****Revision Effective Date**

Helicobacter Pylori Infection Testing

For services performed on or after 10/01/2019

**Proposed LCD in Comment Period**

N/A

**Revision Ending Date**

N/A

**Source Proposed LCD**

DL37626

**Retirement Date**

N/A

**AMA CPT / ADA CDT / AHA NUBC Copyright Statement**

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**Notice Period Start Date**

04/11/2019

**Notice Period End Date**

05/26/2019

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**CMS National Coverage Policy**

Title XVIII of the Social Security Act, §1862(a)(1)(A). Allows coverage and payment for only those services that are considered to be reasonable and necessary.

Title XVIII of the Social Security Act, §1833(e). Prohibits Medicare payment for any claim which lacks the necessary

information to process the claim.

42 Code of Federal Regulations (CFR) 410.32(a). Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions.

CMS On-Line Manual, Publication 100-02, Medicare Benefit Policy Manual, Chapter 15, §§80.0, 80.1.1, 80.2. Clinical Laboratory services.

CMS Internet-Only Manuals, Publication 100-04, Medicare Claims Processing Manual, Chapter 16, §50.5 Jurisdiction of Laboratory Claims, 60.12 Independent Laboratory Specimen Drawing, 60.2. Travel Allowance.

CMS Internet Online Manual Pub. 100-04 (Medicare Claims Processing Manual), Chapter 23 (Section 10) "Reporting ICD Diagnosis and Procedure Codes"

## Coverage Guidance

### Coverage Indications, Limitations, and/or Medical Necessity

This policy provides limited coverage for *Helicobacter pylori* (*H. pylori*) infection testing by carbon isotope ( $^{13}\text{C}$  or  $^{14}\text{C}$ ) urea breath testing or stool antigen testing. This policy also denies coverage for *H. pylori* serology testing, TZAM *H. pylori* multiplex PCR testing, plasma pepsinogen II testing, tonsillar *H. pylori* colonization, IL1B-31>T polymorphism testing for *H. pylori*, tumor necrosis factor-alpha (TNF $\alpha$ ), and AmHPR *Helicobacter* antibiotic resistance next generation sequencing panel testing.

### Summary of Evidence

This policy is consistent with guidelines of the American Gastroenterological Association and the American College of Gastroenterology.<sup>3,4</sup> in younger patients without "alarm" symptoms (e.g., weight loss, progressive dysphagia, recurrent vomiting, evidence of GI bleeding, or family history of UGI cancer)<sup>20</sup>. Endoscopy with biopsy is recommended for patients >55 years of age and younger patients with alarm symptoms.<sup>2,5</sup>

Multiple Food and Drug Administration (FDA) cleared urea place.<sup>6,8</sup> (Halyard Health, Alpharetta, GA).

A stool antigen test, cleared by the FDA, may be used for initial diagnosis, therapeutic monitoring and eradication confirmation in adults and children. The HpSA<sup>®</sup> test (Meridian Bioscience, Cincinnati, OH) is the only FDA cleared stool antigen test in the US. All others use analyte specific reagents (ASR) or are laboratory developed tests (LDTs). The stool antigen test is based on the passage of *H. pylori* bacteria and *H. pylori* antigens in the GI tract, and their detection by immunoassay which translates into the detection of an active infection. The test does not require fasting or an instrument for analysis, does not have adverse effects, nor does it depend on a by-product of *H. pylori* and, has the additional advantage that testing can be performed while patients are on proton pump inhibitor (PPI), bismuth or H2 blockers.

Confirmation of the presence of *H. pylori* bacterium can be determined invasively on endoscopic biopsy followed by rapid urease testing (CLOtest™ PyloriTek™, Hpfast™), by histology which on occasion may require special stains or immunohistochemistry, or culture.

More than 90% of gastroduodenal ulcers are associated with *H. pylori* infection. The ACG guidelines recommend that all person suspected of having peptic ulcer disease should be tested for *H. pylori* regardless of whether they are concurrently taking non-steroidal anti-inflammatory drugs (NSAIDs), as *H. pylori* and NSAIDs are independent risk factors for the development of peptic ulcer disease. Antibiotic therapy is indicated for all *H. pylori* infected ulcer patients together with acid-suppressing drugs to facilitate symptom relief and healing. The ACG also recommend post-treatment testing, by the stool antigen test or the urea breath test, in ALL patients treated for *H. pylori* infection<sup>3</sup>.

With an *H. pylori* prevalence of up to 30-40% in the US, it is not surprising that 30-40% of patients undergoing bariatric surgery are infected with *H. pylori*.<sup>9</sup> Because *H. pylori* infection may increase the risk of post-operative marginal ulcers, noninvasive *H. pylori* infection testing is recommended as part of the routine pre-operative evaluation of patients before bariatric surgery.

The AGA and ACG no longer recommend *H. pylori* serology testing because it is not a test of active infection. Although a negative serology for *H. pylori* antibody can be used to rule out infection, a positive serology indicates *H. pylori* exposure at some time in the past, not whether the patient has current infection. Studies suggest that nearly 50% of person with positive *H. pylori* serology do not have active infection.<sup>3</sup> Furthermore, serology cannot be used to show that *H. pylori* infection has been successfully eradicated after treatment. Antibody levels commonly remain elevated for months to years after treatment.

A reliable diagnosis is mandatory for the identification of infection and to confirm eradication of infection. Although bacterial culture from the gastric biopsy is the "gold" standard technique for *H. pylori* identification, and is recommended for antibiotic susceptibility testing, it is not practical for all patients. Although infrequently indicated, quantitative polymerase chain reaction (PCR) on gastric biopsies can be used to detect low bacterial loads, the use of the testing is limited by its high cost.<sup>10</sup> Others have suggested the measurement of decreased plasma pepsinogen II may be a reliable biomarker to confirm successful eradication of *H. pylori* infection.<sup>11</sup> However, studies are with limited numbers of patients, and inconclusive findings.

Others have suggested that *H. pylori* infection plays a role in the development of other conditions. Hwang et al<sup>12</sup>, in a systematic review and meta-analysis, found no evidence that *H. pylori* infection plays a role in the pathogenesis or development of chronic tonsillitis. Gomes et al<sup>13</sup> concluded that recurrent aphthous stomatitis (RAS) ulcers are not associated with the presence of bacteria in the oral cavity and there is no evidence that *H. pylori* infection drives RAS development. Sun et al<sup>14</sup> hypothesized that host genetic factors that control the production of cytokines, including interleukin -1 $\beta$ , which affect susceptibility to many *H. pylori*-related diseases. The authors concluded that the findings of their meta-analysis showed that IL1 $\beta$ -31C>T polymorphism might increase *H. pylori* risk in Asian and Latin American populations, that TNFa-308G>A and -1031T>C polymorphisms may be protective factors against *H. pylori* infection<sup>15</sup>, and that -863C>A may be a risk factor in Asian populations. However, they indicate further studies with different ethnicities and larger samples size are needed to validate their findings.

AmHPR *H. pylori* antibiotic resistance panel testing examines antibiotic resistance to 6 antibiotic types that are currently used in *H. pylori* treatment by means of NGS: 23S rRNA for clarithromycin; gyrA for fluoroquinolones; rdxA for metronidazole; pbp1 for amoxicillin; 16S rRNA for tetracycline, and rpoB for rifabutin. Binh et al<sup>16</sup> stated that metronidazole resistance is a key factor associated with *H. pylori* failure. The authors confirmed that the mutations in rdxA were mainly associated with metronidazole resistance, and mutations in frxA were able to enhance *H. pylori* resistance only in the presence of rdxA mutations. These authors conclude that further work is needed to identify the

role of mutations associated with treatment failure. In a large pilot study by<sup>17</sup> and colleagues on 849 Indonesian dyspeptic patients, authors showed a high prevalence of metronidazole and levofloxacin resistance with low prevalence of clarithromycin, amoxicillin and tetracycline resistance, largely related to local antibiotic consumption. They noted that resistance is primarily due to the *H. pylori* genotype, rather than the human genotype.

Multiple regimens are available for treating *H. pylori* infection. The first-line regimen for *H. pylori* eradication includes proton pump inhibitor (PPI), clarithromycin (CAM), and amoxicillin (AMX), or metronidazole. Proton pump inhibitors (PPIs) suppress acid production in combination with antibiotic treatment. However, the failure rate of triple anti-*H. pylori* therapies has increased up to 30%. The known factors for therapy failure include antibiotic resistance, poor compliance, high gastric acidity, and high bacterial load.

Studies suggest that cytochrome P450 CYP2C19 polymorphism may also play a role in therapy failure. CYP2C19 is implicated in the metabolism of PPIs. What is known is that differences in PPI metabolism lead to variability in gastric acid suppression, with associated variability in gastric pH, and that CYP2C19 polymorphism is highly varied among different ethnic populations. Observational studies suggest that extensive metabolizers (EM) of PPIs have lower eradication rates following standard treatment for *H. pylori* compared to poor metabolizers (PM). Studies suggest that CYP2C19 genotype is a cardinal factor for *H. pylori* eradication in patients taking omeprazole-based or lansoprazole-based triple therapies. In contrast, this polymorphism has no significant effect on the rabeprazole-based or esomeprazole-based triple therapies. However, overall there is conflicting data and meta-analyses that conflict with one another. At the current time, the existing scientific data is insufficient to demonstrate a causal effect.

## **Analysis of Evidence (Rationale for Determination)**

### **Level of Evidence**

Quality of evidence: Mixed

Strength of evidence: Strong

Weight of evidence: Sufficient

Based upon the American College of Gastroenterology 2017 Guidelines, Noridian establishes the following Criteria for coverage for urea breath testing **or** stool antigen testing for active *H. pylori* infection are:

- Evaluation of new onset, uninvestigated dyspepsia in persons younger than 60 years of age without alarm symptoms; or
- All patients with active peptic ulcer disease (PUD), a past history of PUD (unless previous cure of *H. Pylori* infection is documented); or
- Patients with low grade gastric mucosa-associated lymphoid tissue (MALT); or
- Patients with a history of endoscopic resection of early gastric cancer; or
- Patients taking long term low dose aspirin may be considered for testing to reduce the risk of ulcer bleeding; or
- Patients initiating chronic treatment with nonsteroidal anti-inflammatory drugs; or
- Patients with unexplained iron deficiency despite an appropriate workup; or
- Adults with idiopathic thrombocytopenic purpura; or
- Recurrent dyspeptic symptoms suggest reinfection with *H. pylori*; or
- Re-evaluation to assess success of eradication of *H. pylori* infection (no sooner than 4 weeks post-treatment and after PPI therapy has been withheld for 1-2 weeks).

All other H. pylori testing for any other etiology is not reasonable and necessary, and not a Medicare benefit. Some non-covered etiologies including but not limited to the risk of developing dementia, dyspepsia associated with "alarm" markers, recurrent aphthous stomatitis (RAS), onset of new dyspepsia in person aged 55 years or older, and screening of asymptomatic person for H. pylori infection. Upper GI endoscopy is indicated for persons aged 55 years or older because of increased concern for gastric neoplasia.

Note: Either urea breath testing or stool antigen testing for H. pylori is medically indicated; not both tests. Serology is no longer an acceptable non-invasive test H. pylori infection.

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## General Information

### Associated Information

N/A

### Sources of Information

N/A

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## Revision History Information

| REVISION HISTORY DATE | REVISION HISTORY NUMBER | REVISION HISTORY EXPLANATION  | REASON(S) FOR CHANGE  |
|-----------------------|-------------------------|---|---|
| 10/01/2019            | R2                      | 10/01/2019: At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.<br><br>LCD was converted to the "no-codes" format. | <ul style="list-style-type: none"><li>• Revisions Due To Code Removal</li></ul> |
| 05/27/2019            | R1                      | 04/04/2019: Corrected typographical error in title of LCD.  | <ul style="list-style-type: none"><li>• Typographical Error</li></ul>           |

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## Associated Documents

### Attachments

N/A

### Related Local Coverage Documents

Article(s)

A57227 - Billing and Coding: Helicobacter Pylori Infection Testing

A56382 - Response to Comments: Helicobacter Pylori Infection Testing

LCD(s)

DL37626 - Helicobacter Pylori Infection Testing

### **Related National Coverage Documents**

N/A

### **Public Version(s)**

Updated on 09/20/2019 with effective dates 10/01/2019 - N/A

Updated on 04/05/2019 with effective dates 05/27/2019 - 09/30/2019

Updated on 03/28/2019 with effective dates 05/27/2019 - N/A

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## **Keywords**

- Helicobacter
- Pylori
- Infection
- Testing