Clinical Policy: Infectious Disease: Gastroenterologic Lab Testing

Reference Number: TX.CP.MP.304
Effective Date: 03/24

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

I. Description

Infections of the gastrointestinal (GI) tract represent a significant cause of infectious disease worldwide. GI infections can be caused by several pathogen types, including bacteria, viruses, fungi, and parasites (e.g., protozoal illnesses such as giardiasis). Testing methods range from culture and microscopy to immunoassays and advanced molecular diagnostic techniques; technology in this space is evolving rapidly and clinical guidelines can lag as a result. This document outlines several common types of GI pathogen tests and guideline or peer-reviewed literature-supported criteria for their appropriate applications.

Gastrointestinal infections, most commonly acute diarrheal infections, lead to many outpatient visits each year. Diagnostic workups for suspected diarrheal infections historically included culture and microscopy as standard of care, but with emerging molecular platforms capable of simultaneously evaluating many viral, bacterial, and other targets, standard of care is starting to shift, requiring thoughtful approaches to weighing the clinical benefits and limitations of different diagnostic testing strategies.

This policy outlines appropriate use of multi-pathogen panels, as well as diagnostic assays targeted at Helicobacter pylori (H. pylori) given that it is one of the most common chronic infections worldwide. Testing is indicated for individuals with certain GI symptoms, such as peptic ulcer disease, to guide antibiotic treatment and eradication. H. pylori is also linked to gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) in a small subset of infected individuals. Robust clinical guidelines exist for diagnostic testing and treatment of H. pylori infections.

Note: This policy is applicable to laboratory services delivered in an outpatient setting.

II. Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation® that the specific tests noted below are **medically necessary** when meeting the related criteria:

GASTROINTESTINAL PATHOGEN PANEL TESTS

i. Syndromic Multiplex Gastrointestinal Pathogen Panels with 11 or Fewer Targets

A. Syndromic/Multiplex Gastrointestinal Pathogen Panels with 11 or Fewer Targets may be considered medically necessary when:

1. The member presents in the outpatient setting with suspected infectious gastroenteritis, and is in an immunocompromised status (e.g., HIV/AIDS, immunosuppression therapy, primary immunodeficiency), or has experienced recent travel to/contact with travelers from an infectious diarrheal disease-endemic area, Dysentery (presence of blood or mucus in stool), Fever, Dehydration, Abdominal pain/tenderness, Bacteremia, Diarrhea persisting longer than 7 days, has symptoms of enteric fever (i.e., Typhoid/paratyphoid fever); and
2. Results of the testing will influence the member's clinical management.

B. The use of Syndromic/Multiplex Gastrointestinal Pathogen Panels with 11 or Fewer Targets is considered medically necessary once per incident of diarrheal disease, or no more than once per 14-day period.

C. Current evidence does not support Syndromic/Multiplex Gastrointestinal Pathogen Panels with 11 or Fewer Targets for all other indications.

ii. Syndromic Multiplex Gastrointestinal Pathogen Panels with 12 or More Targets

A. Syndromic/Multiplex Gastrointestinal Pathogen Panels with 12 or More Targets may be considered medically necessary when:

1. The member presents in the outpatient setting with suspected infectious gastroenteritis, is in an immunocompromised status (e.g., HIV/AIDS, immunosuppression therapy, primary immunodeficiency), or has recent travel to/contact with travelers from an infectious diarrheal disease-endemic area, Bacteremia, symptoms of enteric fever (i.e., Typhoid/paratyphoid fever); and
2. Results of the testing will influence the member's clinical management.

B. The use of Syndromic/Multiplex Gastrointestinal Pathogen Panels with 12 or More Targets is considered medically necessary once per incident of diarrheal disease, or no more than once per 14-day period.

C. Current evidence does not support Syndromic/Multiplex Gastrointestinal Pathogen Panels with 12 or More Targets for all other indications.

HELICOBACTER PYLORI (H. PYLORI) TESTS

iii. Helicobacter pylori (H. pylori) Urea Breath or Stool Antigen Tests

A. H. pylori Urea Breath or Stool Antigen Tests may be considered medically necessary when:

1. The member displays at least one of the following: active peptic ulcer disease (PUD), Low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma, a history of endoscopic resection of early gastric cancer (EGC), past history of PUD; and
2. Previous cure of H. pylori infection has **not** been documented, the member has dyspepsia, is younger than 60 years of age, **and d**oes **not** have dyspepsia alarm features (e.g., unintended weight loss, gastrointestinal bleeding, palpable mass or lymphadenopathy), has **not** undergone previous investigation for dyspepsia (i.e., has uninvestigated dyspepsia); or
3. The member is initiating prophylactic low-dose aspirin (e.g., following a major cardiovascular event), is initiating chronic treatment with a non-steroidal anti-inflammatory drug (NSAID), has unexplained iron deficiency (ID) anemia despite an appropriate evaluation, or is an adult with idiopathic thrombocytopenic purpura (ITP).

B. Current evidence does not support H. pylori Urea Breath or Stool Antigen Tests for all other indications, including, but not limited to: for the evaluation of individuals with GERD, lymphocytic gastritis, hyperplastic gastric polyps, or hyperemesis gravidarum, asymptomatic individuals with a family history of gastric cancer, and children and adolescents with functional abdominal pain or short stature.

iv. **Helicobacter pylori (H. pylori) Antibody Tests**

Current evidence does not support H. pylori Antibody Tests for all other indications.

III. Notes and Definitions

A. Uninvestigated dyspepsia refers to dyspepsia that has not already been evaluated via investigations such as upper GI endoscopy and/or is not already classified as functional/organic dyspepsia.

B. Dyspepsia alarm features/symptoms include vomiting, bleeding or anemia, abdominal mass or unintended weight loss, and dysphagia.

C. Symptoms of enteric fever include high fever, abdominal pain, constipation followed by diarrhea (sometimes bloody), rash characterized by flat "rose spots" on abdomen and chest, confusion due to fever, hepatosplenomegaly, GI bleed/perforation. Travel is also a risk factor to consider in patients presenting with fever or flu-like illness after travel or contact with a traveler from endemic areas.

D. Gastroenteritis is characterized by vomiting and/or diarrhea.

IV. Background and Rationale

A. Syndromic/Multiplex Gastrointestinal Pathogen Panels of 11 or Fewer Targets; Syndromic/Multiplex Gastrointestinal Pathogen Panels of 12 or More Targets

American College of Gastroenterology (ACG)

ACG makes the following general recommendations in their 2016 guidelines regarding diagnostic testing for suspected diarrheal infections:

- Stool diagnostic studies may be used if available in cases of dysentery, moderate-to-severe disease, and symptoms lasting >7 days to clarify the etiology of the patient's illness and enable specific directed therapy. (Strong recommendation, very low level of evidence)

The guideline acknowledges the benefit of multiplex molecular testing for diarrheal disease, but does not provide specific guidance regarding recommended panel content.

"Diarrheal disease by definition has a broad range of potential pathogens particularly well suited for multiplex molecular testing. Several well-designed studies show that molecular testing now surpasses all other approaches for the routine diagnosis of diarrhea." (p. 606)

Regarding repeat testing for persistent symptoms, the ACG guideline states:

- Serological and clinical lab testing in individuals with persistent diarrheal symptoms (between 14 and 30 days) is not recommended. (Strong recommendation, very low level of evidence) (p. 611)

Infectious Diseases Society of America (IDSA)

In their 2017 guidelines for infectious diarrhea, the IDSA stated the following: "Although the majority of diarrheal illnesses are self-limited and identification of the infectious etiology often has little value to these individual patients, for certain infections, an organism-specific diagnosis is important to guiding clinical management. However, testing all patients with acute diarrhea for these pathogens would be inefficient… Restricting testing to patients with bloody stools, fever, or abdominal tenderness can increase the likelihood of identifying a bacterial pathogen" (p. e60)

The IDSA outlines several highly specific clinical recommendations regarding diagnostic evaluation for specific pathogens and/or testing methods based on the presentation of a patient with suspected infectious diarrhea. They also summarize many exposures or conditions and the pathogens associated with each (Table 2, p. e48).

Among these pathogen associations, no exposures or situations included are associated with more than 11 pathogens, outside of "travel to a resource-challenged country". Additionally, the guideline recommends considering a "broader set of bacterial, viral, and parasitic agents" for patients with immunocompromisation/AIDS, suspected disease outbreak (for the purposes of public health coordination), and suspected enteric fever or diarrhea with bacteremia (p. e47).

B. Helicobacter pylori (H. pylori) Urea Breath or Stool Antigen Tests

American College of Gastroenterology (ACG)
In their 2017 guidelines, the ACG makes the following recommendations regarding the indications for testing for and treating H. pylori infection:

- All patients with active peptic ulcer disease (PUD), a past history of PUD (unless previous cure of H. pylori infection has been documented), low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma, or a history of endoscopic resection of early gastric cancer (EGC) should be tested for H. pylori infection (strong recommendation, quality of evidence: high for active or history of PUD, low for MALT lymphoma, low for history of endoscopic resection of EGC).
- In patients with uninvestigated dyspepsia who are under the age of 60 years and without alarm features, non-endoscopic testing for H. pylori infection is a consideration (conditional recommendation, quality of evidence: high for efficacy, low for the age threshold).
- Patients with typical symptoms of gastroesophageal reflux disease (GERD) who do not have a history of PUD need not be tested for H. pylori infection.
- In patients taking long-term low-dose aspirin, testing for H. pylori infection could be considered to reduce the risk of ulcer bleeding. Those who test positive should be offered eradication therapy (conditional recommendation, moderate quality of evidence).
- Patients initiating chronic treatment with a non-steroidal anti-inflammatory drug (NSAID) should be tested for H. pylori infection (strong recommendation, moderate quality of evidence).
- Patients with unexplained iron deficiency (ID) anemia despite an appropriate evaluation should be tested for H. pylori infection (conditional recommendation, high quality of evidence).
- Adults with idiopathic thrombocytopenic purpura (ITP) should be tested for H. pylori infection (conditional recommendation, very low quality of evidence).
- There is insufficient evidence to support routine testing and treating of H. pylori in asymptomatic individuals with a family history of gastric cancer or patients with lymphocytic gastritis, hyperplastic gastric polyps and hyperemesis gravidarum (no recommendation, very low quality of evidence). (p.213-214)

European Society for Paediatric Gastroenterology Hepatology and Nutrition/North American Society for Pediatric Gastroenterology, Hepatology and Nutrition
The following ESPGHAN/NASPGHAN recommendations made in 2016 are pertinent to the testing of children and adolescents for H. pylori infection (see publicly available guideline for full list of recommendations):

- We recommend against diagnostic testing for H pylori infection in children with functional abdominal pain.
- We recommend against diagnostic testing for H pylori infection as part of the initial investigation in children with iron deficiency anemia.
- We suggest that noninvasive diagnostic testing for H pylori infection may be considered when investigating causes of chronic immune thrombocytopenic purpura (ITP).

- We recommend against diagnostic testing for H pylori infection when investigating causes of short stature. (p. 992)

C. Helicobacter pylori (H. pylori) Antibody Tests

American College of Gastroenterology (ACG)
In their 2017 guidelines, the ACG acknowledges a rare appropriate indication for H. pylori antibody testing in patients with documented PUD; however, the ideal test is one that can differentiate between active/current and past infection:
"Ideally, tests which identify active infection such as a urea breath test, fecal antigen test, or when endoscopy is performed, mucosal biopsy-based testing should be utilized." (p. 216)

V. Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2022, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

Table 1

Criteria Sections	Lab Tests	References
Syndromic Multiplex Gastrointestinal Pathogen Panels with 11 or Fewer Targets	Enteric Bacterial Panel by PCR	1, 2
	Gastrointestinal Pathogen Panel, Real-Time PCR	
Syndromic Multiplex Gastrointestinal Pathogen Panels with 12 or More Targets	Gastrointestinal (GI) Panel	
	GI assay (Gastrointestinal Pathogen with ABR)	
Helicobacter pylori (H. pylori) Urea Breath or Stool Antigen Tests	Helicobacter pylori Breath Test	3, 4

Criteria Sections	Lab Tests	References
	Helicobacter pylori Stool Antigen	
Helicobacter pylori (H. pylori) Antibody Tests	Helicobacter pylori Antibody, IgG, Serum	3

Table 2

CPT® Codes	Description
83013	Helicobacter pylori, blood test analysis for urease activity, non-radioactive isotope (eg, C-13)
83014	Helicobacter pylori; breath test analysis for urease activity, non-radioactive isotope (eg, C-13)
86677	Antibody; Giardia lamblia
87338	Infectious agent antigen detection by immunoassay technique (eg, enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]), qualitative or semiquantitative; Entamoeba histolytica group
87339	Infectious agent antigen detection by immunoassay technique (eg, enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]), qualitative or semiquantitative; Helicobacter pylori, stool
87493	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, quantification
87498	Infectious agent detection by nucleic acid (DNA or RNA); cytomegalovirus, quantification
87500	Infectious agent detection by nucleic acid (DNA or RNA); enterovirus, amplified probe technique, includes reverse transcription when performed
87505	Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, for multiple types or sub-types, includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, each additional influenza virus type or sub-type beyond 2 (List separately in addition to code for primary procedure)
87506	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (eg, Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 3-5 targets
87507	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (eg, Clostridium difficile, E. coli, Salmonella, Shigella, norovirus,

CPT® Codes	Description
	Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 6-11 targets
87551	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria species, direct probe technique
87556	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria tuberculosis, direct probe technique
87561	Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria avium-intracellulare, direct probe technique
87651	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, direct probe technique
87652	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, amplified probe technique
87653	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, quantification
87797	Infectious agent detection by nucleic acid (DNA or RNA); Zika virus, amplified probe technique
87798	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; direct probe technique, each organism
87799	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; amplified probe technique, each organism
87800	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; quantification, each organism
87801	Infectious agent detection by nucleic acid (DNA or RNA), multiple organisms; direct probe(s) technique
0369U	Infectious agent detection by nucleic gi pathogen 31 org&21 arg

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed	02/24	02/24

References

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2. Shane AL, Mody RK, Crump JA, Tarr PI, Steiner TS, Kotloff K, Langley JM, Wanke C, Warren CA, Cheng AC, Cantey J, Pickering LK. 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea. Clin Infect Dis. 2017 Nov 29;65(12):e45-e80. doi: 10.1093/cid/cix669. PMID: 29053792; PMCID: PMC5850553.

3. Chey, William D MD, FACG1; Leontiadis, Grigorios I MD, PhD2; Howden, Colin W MD, FACG3; Moss, Steven F MD, FACG4. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. American Journal of Gastroenterology 112(2):p 212-239, February 2017. DOI: 10.1038/ajg.2016.563
4. Jones NL, Koletzko S, Goodman K, Bontems P, Cadranel S, Casswall T, Czinn S, Gold BD, Guarner J, Elitsur Y, Homan M, Kalach N, Kori M, Madrazo A, Megraud F, Papadopoulou A, Rowland M; ESPGHAN, NASPGHAN. Joint ESPGHAN/NASPGHAN Guidelines for the Management of Helicobacter pylori in Children and Adolescents (Update 2016). J Pediatr Gastroenterol Nutr. 2017 Jun;64(6):991-1003. doi: 10.1097/MPG.0000000000001594. PMID: 28541262.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended

to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members/enrollees, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.