02.04.84 Serologic Testing for Biomarkers of Irritable Bowel Syndrome (IBS)

Original Effective Date: April 2011

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DISCLAIMER/INSTRUCTIONS FOR USE

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This Medical Policy document describes the status of medical technology at the time the document was developed. Since that time, new technology may have emerged, or new medical literature may have been published. This Medical Policy will be reviewed regularly and updated as scientific and medical literature becomes available; therefore, policies are subject to change without notice.

Related Policies:

02.04.33. Fecal Calprotectin and Lactoferrin Testing in the Diagnosis and Management of Inflammatory Bowel Disease

Summary

Description

Individuals who suffer from cramping, abdominal pain, bloating, gas, diarrhea, and/or constipation may have a chronic condition of the large intestine called irritable bowel syndrome (IBS). The Rome criteria is a set of symptom-based criteria that is utilized to make a diagnosis of IBS. The IBSDetex™, ibs-smart® and IBSchek® are three serologic marker tests currently on the market intended to aid providers in diagnosing and ruling out IBS through detection of circulating anti-CdtB and anti-vinculin antibodies. The IBSDetex and ibs-smart collection kits use a blood sample collected via venipuncture. The IBSchek is a home-based capillary blood sample collection.

Summary of Evidence

For individuals who have suspected or confirmed irritable bowel syndrome (IBS) who utilize serological testing for biomarkers of irritable bowel syndrome (for example, CdtB and anti-vinculin), using tests such as, IBSDetex, ibs-smart or IBSchek. no relevant evidence was identified. Relevant outcomes are test validity, symptoms, change in disease status, QOL, hospitalizations, and medication use. No studies have directly evaluated whether using serological testing for IBS biomarkers (for example, CdtB and anti-vinculin), using tests such as, IBSDetex, ibs-smart or IBSchek improves the health outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Additional Information

Not applicable.

OBJECTIVE

The objective of this evidence review is to determine whether serological testing for biomarkers of irritable bowel syndrome (for example, CdtB and anti-vinculin), using tests such as, IBSDetex, ibs-smart or IBSchek improves the net health outcome in individuals with or suspected of having inflammatory bowel disease.

PRIOR APPROVAL

Not applicable.

POLICY

Serological testing for biomarkers of irritable bowel syndrome (i.e., CdtB and anti-vinculin), using tests such as, IBSDetex, ibs-smart or IBSchek, is considered **investigational** for screening, diagnosis, or management of irritable bowel syndrome because the evidence is insufficient to determine the technology results in an improvement in the net health outcomes.

Note: This evidence review does not address any other type of testing for IBS including breath tests, fecal analysis, gene expression profiling or imaging.

POLICY GUIDELINES

Note:
Iowa House File 2668 (Iowa Code section 514C.36) requires that certain health plans issued or renewed on or after January 1, 2025 “provide coverage for biomarker testing for the purposes of diagnosing, treating, appropriately managing, or monitoring a disease or condition in a covered person when the biomarker testing has demonstrated clinical utility.” Iowa House File 2668 defines clinical utility as ”sufficient medical and scientific evidence indicating that the use of a biomarker test will provide meaningful information that affects treatment decisions and guides improvement of net health outcomes, including an improved quality of life or longer survival.” Wellmark has reviewed this Medical Policy in light of Iowa House File 2668.

Definitions

Biomarker: A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic response to a therapeutic intervention.

Coding

See the Codes table for details.

BACKGROUND

Serological and BioMarker Testing

Serological testing and combined serological testing have been proposed to diagnose and assist in treatment planning for individuals with IBS. Serological testing involves obtaining a blood sample for analysis to determine the presence of antibodies which help identify individuals with IBS.

A test for the measurement of two biomarkers has been developed to reportedly aid in the diagnosis of diarrhea-predominant IBS. The test measures anticytolethal distending toxin B (CdtB) and antivinculin. CdtB is a toxin released by the four main bacteria known to cause gastroenteritis and vinculin is a protein released as a result of nerve and intestinal tissue damage. The test results may indicate the presence of IBS as opposed to IBD. The IBSDetex™, ibs-smart® and IBSchek® are three serologic marker tests currently on the market purposed to aid providers in diagnosing and ruling out IBS through detection of circulating anti-CdtB and anti-vinculin antibodies. The IBSDetex and ibs-smart collection kits use a blood sample collected via venipuncture. The IBSchek is a home-based capillary blood sample collection. Tests provide biomarker levels for clinician interpretation within approximately 2-3 days.

In the United States IBS is estimated to effect 12-15% of the population. IBS is typically symptom management achieved through changes in diet as well as pharmaceuticals, probiotics, and mental health support.

Regulatory Status

Below are some of the identified gastrointestinal tests which have been reviewed by the U.S. Food and Drug Administration (FDA) or the Clinical Laboratory Improvement Amendments (CLIA). (*Please note, this is not an all-inclusive list*)

- Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory developed tests must meet the general regulatory standards. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing.

Test	Manufacturer	Description
IBSchek®	Commonwealth Diagnostics International	According to the manufacturer, IBSchek® Capillary Kit is a diagnostic blood test designed to help patients and physicians quickly diagnose diarrhea-predominant or mixed-symptom IBS (IBS-D/M). Symptoms of this chronic ailment often occur following an incident of acute gastroenteritis (food poisoning). IBSchek is available with direct patient access with results in just a few days. It was clinically validated in 2015 and revalidated internationally and is available in the USA.
IBSDetex™	Quest Diagnostics	Quest details, “physicians and their patients with a quick, simple, first-line diagnostic test for post-infectious IBS-D

Test	Manufacturer	Description
		(diarrhea-predominant IBS) and IBS-M (IBS with both diarrhea and constipation)."
IBS-Smart™	Gemelli Biotech	Gemelli Biotech reports "ibs-smart measures the levels of two validated IBS biomarkers, anti-CdtB and anti-vinculin. These biomarkers are elevated in a majority of IBS patients with diarrheal symptoms and can diagnose diarrhea-predominant or mixed-type IBS (IBS-D or IBS-M). These biomarkers are not commonly elevated in patients with constipation-predominant IBS (IBS-C). Only a licensed physician can order ibs-smart and diagnose IBS."

Note: Multiple laboratory tests, some general and some proprietary, have been utilized for the diagnosis and ongoing management of irritable bowel disease. Many individual tests do not require FDA approval for laboratory practices.

RATIONALE

This evidence review was created in April 2011 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through October 2025.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

IBSDetex, ibs-smart® and IBSchek®

Clinical Context and Test Purpose

Serological testing using IBSDetex, ibs-smart® and IBSchek® are three serologic markers intended to aid providers in screening for, differential diagnosing and management of IBS through detection of circulating anti-CdtB and anti-vinculin antibodies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with suspected or confirmed IBS.

Interventions

The test being considered is IBSDetex, ibs-smart® and IBSchek®.

Comparators

Rome criteria: An international effort to create criteria based on scientific data to help in the diagnosis and treatment of functional gastrointestinal disorders. These criteria include abdominal pain and discomfort lasting on average of at least 1 day a week in the last 3 months, associated with at least 2 of the following factors: Pain and discomfort are related to defecation, the frequency of defecation is altered, or stool consistency is altered.

Outcomes

Relevant outcomes are test validity, symptoms, change in disease status, QOL, hospitalizations, and medication use.

Study Selection Criteria

For the evaluation of the clinical validity of the fecal calprotectin test, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology.
- Included a suitable reference standard (endoscopy).
- Patient/sample clinical characteristics were described.
- Patient/sample selection criteria were described.

Clinically Valid

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

No studies on the sensitivity and specificity of serological testing for IBS biomarkers (for example, CdtB and anti-vinculin) compared with a reference standard were identified.

Review of Evidence

We did not identify any RCTs or systematic reviews of IBSDetex, ibs-smart® and IBSchek® that reviewed for outcomes of interest, such as test validity, symptoms, medication use, response to treatment, change in disease status, recurrence and QOL**.**

Clinically Useful

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, or avoid unnecessary therapy or testing.

Direct Evidence

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

Section Summary: IBSDetex, ibs-smart® and IBSchek®

No studies were identified that have directly evaluated whether using serological testing using IBSDetex, ibs-smart® and IBSchek® screening for, diagnosing and manage IBS through detection of circulating anti-CdtB and anti-vinculin antibodies status improves the health outcomes such as change in disease status and morbid events.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Gastroenterological Association (AGA)

In 2019, the AGA published a Clinical Practice Guideline on the Laboratory Evaluation of Functional Diarrhea and Diarrhea-Predominant Irritable bowel Syndrome in Adults (IBS-D) which stated, "Recommendation 7. In patients presenting with chronic diarrhea, the AGA makes no recommendation for the use of currently available serologic tests for diagnosis of IBS. (No recommendation; knowledge gap)."

In 2022 the AGA published 2 of their Clinical Practice Guideline on the Pharmacological Management of Irritable Bowel Syndrome With Constipation and the Guideline on the Pharmacological Management of Irritable Bowel Syndrome With Diarrhea addressed the following limitations and evidence gaps on biomarkers: "A continued unmet need in IBS clinical trials is the lack of a biomarker that can embody the different pathophysiologic mechanisms of IBS or that can reliably predict treatment response to medications that have different predominant mechanisms of action (e.g., normalizing bowel habits and visceral analgesic) and a need for clinically effective treatments that relieve multiple symptoms. Dietary modification and behavioral treatments have shown beneficial effects in patients with IBS and should be considered on an individual basis, as these may be used in conjunction with pharmacological therapies. The efficacy of these interventions alone or in conjunction with pharmacological therapies was outside the scope this guideline. A recent AGA guideline on probiotics highlighted the evidence gaps in the use of probiotics in patients with IBS, and concluded that future, larger, and high-quality studies are needed. In addition, studies evaluating the synergistic effects of combined treatment in IBS, which is often used in patients with moderate to severe symptoms in clinical practice, and better comparative effectiveness studies in IBS are needed."

American College of Gastroenterology (ACG)

In 2021, the ACGs Clinical Guideline on the Management of Irritable Bowel Syndrome does not provide any recommendations on the use of biomarkers in the diagnosis, treatment, and management of IBS. They do however, state, "A major shortfall in making the diagnosis of IBS is the absence of biomarkers."

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

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CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
	0164U	Gastroenterology (irritable bowel syndrome [IBS]), immunoassay for anti-CdtB and anti-vinculin antibodies, utilizing plasma, algorithm for elevated or not elevated qualitative results (*May be utilized for IBS-Smart*)
	0176U	Cytolethal distending toxin B (CdtB) and vinculin IgG antibodies by immunoassay (i.e., ELISA) (*May be utilized for IBSchek)*
HCPCS		
	No code(s)	
Type of Service	Laboratory	
Place of Service	Outpatient	

POLICY HISTORY

Date	Reason	Action
October 2025	Annual Review	Policy Renewal
October 2024	Annual Review	Policy Renewal

Date	Reason	Action
October 2023	Annual Review	Policy Revised, New Medical Policy Created, Content Moved from 02.04.33 Fecal Calprotectin and Lactoferrin Testing in the Diagnosis and Management of Inflammatory Bowel Disease
October 2022	Annual Review	Policy Renewal
October 2021	Annual Review	Policy Revised
October 2020	Annual Review	Policy Revised
June 2020	Interim Review	Policy Revised
October 2019	Annual Review	Policy Revised
October 2018	Annual Review	Policy Revised
October 2017	Annual Review	Policy Revised
October 2016	Annual Review	Policy Revised
November 2015	Annual Review	Policy Revised
December 2014	Annual Review	Policy Renewed
February 2014	Annual Review	Policy Renewed
March 2013	Annual Review	Policy Renewed
March 2012	Annual Review	Policy Renewed
April 2011	Literature Review	New Policy

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

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