Name of Policy:
Immunoassay/Immunochemical Fecal Occult Blood Testing

Policy #: 192  Latest Review Date: March 2010
Category: Laboratory  Policy Grade: Effective 02/06/2013:
Active Policy but no longer scheduled for regular literature reviews and updates.

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
**Description of Procedure or Service:**
Immunoochemical fecal occult blood tests (iFOBT) are proposed for colorectal cancer screening as an alternative to guaiac-based FOBT. iFOBT does not have dietary or drug restrictions prior to sample collection, and possibly simpler sampling instructions, which may lead to higher patient compliance.

Colorectal cancers and some precancerous adenomas often bleed periodically. Consequently, a small amount of blood in the stool (fecal occult blood) in the absence of other explanatory conditions is a marker for neoplasia. Immunoochemical fecal occult blood tests (iFOBT) are used for the colorectal cancer screening by employing antibodies to detect the globin portion of human hemoglobin in stool. Because globin is degraded during passage through the upper gastrointestinal tract, the iFOBT is specific for bleeding that is limited to the colon and rectum.

Guaiac fecal occult blood testing (gFOBT) has been the standard test used for screening but requires complicated dietary and drug restrictions prior to testing and sampling instructions may limit patient compliance. iFOBTs offer testing without dietary or drug restrictions and may offer simpler sampling instructions.

The iFOBTs approved by the U.S. Food and Drug Administration (FDA) for marketing in the United States are InSure™ (Enterix, Inc.), Instant-View® (Alpha Scientific Designs, Inc.), immoCARE (Care Products, Inc.), and MonoHaem® (Chemicon International, Inc.). The tests require sample collection from 1 stool (Instant-View®, immoCARE), 2 stools (InSure™), or 3 stools (MonoHaem®). The test formats for several iFOBTs require minimal processing and involve developing a test strip with controls and reading a color reaction. In the case of the InSure™ iFOBT, all tests are developed by Quest Diagnostic Laboratories through an exclusive arrangement. For InSure™, a dry stool specimen is not required, and the sample may be collected by brushing the surface of the stool while in the toilet bowl water which may be more agreeable to the patient.

A number of additional iFOBTs have been cleared through the the FDA 510(k) process. Some (not the entire list) of these include Hema-Screen Specific (Immunostics), Innovacon Flipcard Fecal Occult Blood Test (Innovacon), OC Auto Micro FOB Test (Polymedco and Eiken), FlexSure OBT (SmithKline Diagnostics), Teco Rapid FOB Card Test (TECO Diagnostics), QuickVue (Quidel) and inSure II (Enterix, Inc.). In addition, the iScreen FOB is noted to be cleared by FDA and waived under Clinical Laboratory Improvement Amendments (CLIA), and thus available for point-of-care testing.

**Policy:**
Immunooassay/Immunoochemical fecal occult blood tests, for routine physical examination and in screening for colorectal cancer or other sources of lower gastrointestinal bleeding meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage.

Please verify routine and screening benefits coverage for each contract.
Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Colorectal cancer (CRC) is the fourth most common form of cancer and the second leading cause of cancer deaths in the United States. In 2001, over 135,000 cases of CRC were diagnosed and an estimated 57,000 deaths occurred in the United States. The primary risk factor for CRC is age; more than 90% or cases are diagnosed in adults over the age of 50. It is estimated that at age 50, a person has about a 5% remaining lifetime risk of being diagnosed with colorectal cancer. About 20% of cases occur in persons with specific risk factors (e.g., inflammatory bowel disease), and about 6% arise from persons with uncommon genetic syndromes such as familial adenomatous polyposis. The incidence also is increased in individuals with a personal or family history of colorectal cancer or polyps.

Key Points:
Colorectal cancer (CRC) is the fourth most common form of cancer and the second leading cause of cancer deaths in the United States. In 2001, over 135,000 cases of CRC were diagnosed and an estimated 57,000 deaths occurred in the United States. The primary risk factor for CRC is age; more than 90% or cases are diagnosed in adults over the age of 50. It is estimated that at age 50, a person has about a 5% remaining lifetime risk of being diagnosed with colorectal cancer. About 20% of cases occur in persons with specific risk factors (e.g., inflammatory bowel disease), and about 6% arise from persons with uncommon genetic syndromes such as familial adenomatous polyposis. The incidence also is increased in individuals with a personal or family history of colorectal cancer or polyps.

The American Cancer Society states that fecal occult blood testing is non-invasive, is done in the privacy of the home, and can be a useful method of screening when done correctly on an annual basis. The conventional gFOBT has some drawbacks; it is not very sensitive and can only detect tumors that are bleeding at the time of sampling. This test can also give false positive results. Specific instructions for the gFOBT include avoiding non-steroidal anti-inflammatory drugs seven days prior to testing, avoiding vitamin C for three days prior to testing, and avoiding red meats for three days before testing. Sampling also requires specimens from three stools. Immunochemical tests are more specific and have less false positives results. These tests do not require dietary restrictions, and only require only two stool specimens. Immunochemical tests also are unable to detect a tumor that is not bleeding. The experts reported to CMS that this technique could be added to colorectal cancer screening guidelines as this test was more patient-friendly and was likely to be equal or better in sensitivity and specificity.

Concerns with iFOBT include the test is more expensive than the guaiac smear method and that the test may be too sensitive. iFOBT detects small amounts of blood that may not actually be indicative of cancer and may lead to further and unnecessary diagnostic procedures. It is hoped that more people will be encouraged to be screened.

Centers for Medicare and Medicaid Services (CMS), November 2003, has also issued a coverage statement that there is adequate evidence to determine that the immunoassay fecal occult blood test is an appropriate and effective colorectal cancer screening test for Medicare beneficiaries aged 50 and older.

The Blue Cross Blue Shield Association Technology Evaluation Center (TEC) issued the following opinion in June 2004: “the use of immunochemical fecal occult blood testing for
colorectal cancer screening does not meet the TEC criteria”. This was based on the lack of evidence in the research to support all five criteria.

Currently, guaiac and immunochemical are the two main types of tests used to examine stool for the presence of blood. The guaiac stool tests are the most commonly used tests and can yield false-positive results if certain foods, vitamins or drugs are consumed days prior to the exam. Recent studies show that fewer than 40% of the people who should be screened do so on a regular basis. Reviews of newer, less invasive types of tests are being evaluated for screening for CRC, such as virtual colonoscopy, and stool DNA tests. The recommendations for screening from the ACS do remain the same for individuals over the age of 50 with one of five screening options: fecal occult blood test every year, or flexible sigmoidoscopy every 5 years, or fecal occult blood test every year plus flexible sigmoidoscopy every 5 years, or double contrast barium enema every 5 years or colonoscopy every 10 years.

2009 Update
At this time, there are no randomized clinical trials of iFOBT for the prevention of colon cancer mortality. However, a large body of indirect evidence has been published and it has been reviewed in recent guideline documents from the U.S. Preventive Services Task Force (USPSTF) and the joint guideline from the American Cancer Society and U.S. Multi-Society Task force on Colorectal Cancer. Most of these studies compare various types of FOBTs in comparison to a reference standard of colonoscopy or sigmoidoscopy along with clinical follow-up for a single episode of screening. Measures of sensitivity and specificity can be calculated from these types of studies, but it is difficult to ascertain the effectiveness of an overall screening program which would consist of annual or other time interval screening.

The recommendation of the U.S. Preventive Services Task force regarding iFOBT appears to be an endorsement of iFOBT. The clinical summary section of the document states that high-sensitivity FOBT receives a Grade A recommendation. iFOBT is not specifically mentioned in the guideline statement. However, in the accompanying systematic review, the abstract states that four fecal immunochemical tests “have superior sensitivity… and some have similar specificity… to the Hemoccult II fecal occult blood test….”. Later in the abstract it states that “Fecal tests with better sensitivity and similar specificity are reasonable substitutes for traditional fecal occult blood test.” However, it appears that the traditional (non-high sensitivity) fecal occult blood test is not recommended. In a qualitative ranking of the various tests, iFOBT was considered less than or equal in sensitivity to Hemoccult SENSA (a high-sensitivity guaiac-based FOBT) and more specific.

The American Cancer Society/Multi-Society Task Force reviewed 6 studies that compared different iFOBT with Hemoccult SENSA, since SENSA has the highest sensitivity of currently marketed guaiac-based FOBT. Their overall conclusion was that there was no clear pattern of superior performance in overall test characteristics between the two tests. Their joint guideline contains an unambiguous endorsement of iFOBT, along with endorsements of high-sensitivity guaiac-based FOBT and stool DNA tests.

The U.S. Preventive Services Task Force systematic review found 9 fair- or good-quality cohort studies evaluating iFOBT in over 86,000 persons. This review tends to compare various iFOBT
to traditional guaiac-based (non-high sensitive) FOBT. Overall iFOBT’s had higher sensitivity for colorectal cancer (61% to 91%) than had been reported for Hemoccult II (25% to 38%) in another systematic review. Estimated specificity varied across types of tests, from 91% to 98%, which was lower than the specificity of Hemoccult II. They note that the different iFOBT tests cannot be clearly analyzed as a class. Several of the studies reviewed were of tests that are not marketed in the U.S.

A study by Allison (included in the ACS and USPSTF reviews) of the FlexSure OBT, which is available and marketed in the U.S., showed a sensitivity of 82% and specificity of 97% for left-sided (i.e., detectable by sigmoidoscopy) colorectal cancer, which was better for both characteristics than Hemoccult Sena (64% and 90%, respectively), a high-sensitivity test, in the same patients. However, sensitivity of the iFOBT was worse for large adenomas (29.5% versus 41.3%), although specificity was better. In this study, predictive values and likelihood ratios were better for FlexSure; but as noted elsewhere, these performance characteristics cannot be assumed for all iFOBTs. (The USPSTF report noted that estimated specificity varied (91% to 98%) across fecal immunochemical tests.) The study by Allison also reported higher sensitivities than some other studies, which the authors felt was due at least in part to collecting three specimens, instead of one.

2010 Update
There continue to be studies comparing different iFOBT. Hundt and colleagues conducted a prospective multicenter screening study in Germany that evaluated the performance of 6 iFOBT and a guiaic-based FOBT. The iFOBT evaluated were Bionexia FOBplus (DIMA, Germany), Bionexia Hb/Hp Complex (DIMA, Germany), PreventID CC (Preventis, Germany), ImmoCARE-C (CAREagnostica Germany), FOB advanced (Ultimed, Germany) and QuickVue iFOB (Quidel, San Diego, CA). Only the QuickVue test has been approved by the FDA. The study included average-risk individuals (i.e., no inflammatory bowel disease, visible rectal bleeding or other conditions indicating possible increased risk) who returned stool samples by the date of their colonoscopy appointment. Colonoscopy served as the gold standard test; these were conducted by physicians blinded to FOBT results. A total of 1319 patients met eligibility criteria and were included in the analysis; 405 (30.7%) had a positive colonoscopy result (detection of any adenoma). An advanced adenoma was detected in 130 (10%) of participants. There was a wide range in the sensitivities and specificities of the iFOBT. Sensitivity for the detection of any adenoma ranged from 11.4% (95% confidence interval [CI] = 8.4-14.9%) for ImmoCARE-C to 58.0% (95% CI = 53.1-62.9%) for Bionexia Hb/Hp Complex. Sensitivity for the detection of advanced adenomas (the authors did not define what they meant by advanced) ranged from 25.4% (95% CI = 18.2-33.8%) for ImmoCARE-C to 71.5% (95% CI = 63.0-79.1%) for Bionexia Hb/Hp Complex. Specificities ranged from 58.5% to 96.7%; only 2 tests (ImmunoCareC and FOB advanced) had specificities above 90%. QuickVue, a test cleared by the U.S. FDA, had a sensitivity of 45.2 (95% CI = 40.3-50.2%) for detecting any adenoma and 56.2 (95% CI = 47.2-64.8%) for detecting an advanced adenoma and a specificity of 70.2% (95% CI = 67.2%-83.2%). The guiaic-based test had a lower sensitivity than any of the iFOBT e.g., 5.4% (95% CI = 3.4-5.8%) for any adenoma and a specificity of 95.9% (95% CI = 94.4-97.1%) which was higher than all but one of the iFOBT.
**Key Words:**
Immunoassay fecal occult blood test, immunochemical fecal occult blood test, iFOBT, guaiac fecal occult blood test, gFOBT, FOBT, fecal occult blood test, QuickVue

**Approved by Governing Bodies:**
InSure™ (Enterix, Inc.), Instant-View® (Alpha Scientific Designs, Inc.), immoCARE (Care Products, Inc.), and MonoHaem® (Chemicon International, Inc.) These tests have all received FDA approval.

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

ITS: Home Policy provisions apply
BellSouth/AT&T contracts: No special consideration
FEP contracts: FEP does not consider investigational. Will be reviewed for medical necessity
Wal-Mart: Special benefit consideration may apply. Refer to member’s benefit plan.
Pre-certification/Pre-determination requirements: Not applicable

Specific contract exclusions for screening tests/routine examinations may affect coverage eligibility for this test.

**Coding:**
CPT codes: 82274  Blood, occult, by fecal hemoglobin determination by immunoassay, qualitative, feces, 1-3 simultaneous determinations

HCPCS G0328  Colorectal cancer screening; fecal occult blood test immunoassay, 1-3 simultaneous

**References:**


Policy History:
Medical Policy Group, August 2004 (1)
Medical Policy Administration Committee, August 2004
Available for comment August 24-October 7, 2004
Medical Policy Group, August 2006 (1)
Medical Policy Group, February 2009 (4)
Medical Policy Group, March 2010 (3)
Medical Policy Group, February 2013 (3): Effective 02/06/2013: Active Policy but no longer scheduled for regular literature reviews and updates.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.