HEALTH PLANS
UNIVERSITY OF UTAH

Medical Policy

Fecal Elastase (FE-1) Testing

Policy MP-043

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Current Effective Date: 11/25/2024

Disclaimer:

1. Policies are subject to change in accordance with State and Federal notice requirements.
2. Policies outline coverage determinations for U of U Health Plans Commercial, CHIP and Healthy U (Medicaid) plans. Refer to the "Policy" section for more information.
3. Services requiring prior-authorization may not be covered, if prior-authorization is not obtained.
4. This Medical Policy does not guarantee coverage or payment of the service. The service must be a benefit in the member's plan and the member must be eligible for coverage at the time of service. Additional payment guidelines may be applied that are not included in this policy.

Description:

Patients may present for assessment by providers with many symptoms to suggest maldigestion/malabsorption. These symptoms may include greasy, unusually foul-smelling stools, abdominal pain, bloating and gas, weight loss without trying, loose stools or diarrhea or malabsorption. In many instances routine blood or other testing may not identify a cause.

If the diagnosis is unclear or in those without well-established pancreatic disease, an indirect test of pancreas function (fecal elastase-1) to establish the diagnosis of exocrine pancreatic insufficiency (EPI) may be helpful.

Fecal elastase is the most sensitive and specific indirect test of pancreatic function, and the most widely available and commonly performed pancreatic function test in clinical practice. Fecal elastase-1 is an enzymatic product of pancreatic secretion that remains relatively stable during transport through the gastrointestinal tract. There is a direct correlation in pancreatic elastase-1 concentrations in pancreatic fluid and stool. Fecal elastase-1 must be performed on a semi-solid or solid stool specimen. Watery diarrhea may dilute the fecal specimen and produce false-positive results. This limitation can be ameliorated by lyophilizing (concentrating) the stool sample.

Fecal elastase-1 < 200 mcg/g is considered abnormal. Levels < 100 mg/g of stool are more consistent with EPI, while levels of 100 to 200 mg/g of stool are indeterminate for exocrine pancreatic insufficiency. The sensitivity of fecal elastase-1 for mild, moderate, and severe

exocrine pancreatic insufficiency in patients with chronic pancreatitis are 63 and 100 percent, respectively. Fecal elastase has a specificity of 93 percent in patients with exocrine pancreatic insufficiency. Exogenous pancreatic enzyme replacement therapy does not alter fecal elastase test results.

Policy Statement and Criteria

1. Commercial Plans/CHIP

U of U Health Plans covers fecal elastase testing in the assessment of malabsorption in members suspected of possible exocrine pancreatic insufficiency.

U of U Health Plans does not cover fecal elastase testing for any other indication as it considered investigational.

2. Medicaid Plans

Coverage is determined by the State of Utah Medicaid program; if Utah State Medicaid has no published coverage position and InterQual criteria are not available, the U of U Health Plans Commercial criteria will apply. For the most up-to-date Medicaid policies and coverage, please visit their website at: https://medicaid.utah.gov/utah-medicaid-official-publications/ or the Utah Medicaid code Look-Up tool

CPT/HCPCS codes covered by Utah State Medicaid may still require further evaluation to determine medical necessity for coverage.

Clinical Rationale

In a 2018 systematic review and meta-analysis, Vanga et al evaluated the accuracy of measurement of fecal elastase-1 in the detection of exocrine pancreatic insufficiency (EPI). The review included a total of 428 cases of EPI and 673 individuals without EPI (controls), from 14 studies. The assay for elastase-1, compared to secretin stimulation test, identified patients with pancreatic insufficiency with a pooled sensitivity value of 0.77 (95% CI, 0.58-0.89) and specificity value of 0.88 (95% CI, 0.78-0.93). In an analysis of 345 cases of EPI and 312 controls, from 6 studies, the fecal elastase-1 assay identified patients with EPI with a pooled sensitivity value of 0.96 (95% CI, 0.79-0.99) and specificity value of 0.88 (95% CI, 0.59-0.97), compared to quantitative fecal fat estimation. In patients with low pre-test probability of EPI (5%), the fecal elastase-1 assay would have a false-negative rate of 1.1% and a false-positive rate of 11%, indicating a high yield in ruling out EPI but not in detection of EPI. In contrast, in patients with high pre-test probability of EPI (40%), approximately 10% of patients with EPI would be missed (false negatives). The authors found that normal level of elastase-1 (above 200 mcg/g) can rule out EPI in patients with a low probability of this disorder (such as those with irritable bowel syndrome with diarrhea). However, in these patients, an abnormal level of elastase-1 (below 200 mcg/g) has a high false-positive rate.

In a 2014 retrospective study Goepp et al evaluated the frequency of abnormal fecal biomarker results in 2256 records for patients with irritable bowel syndrome (IBS) symptoms and found that 82.8% had at least one abnormal value. 73.1% of records indicated low growth of beneficial bacteria such as

Lactobacillus and Bifidobacterium. Fecal analyses in 14.3% of records showed abnormally elevated eosinophil protein X levels, 12.1% showed elevated calprotectin, and 7.5% showed low pancreatic elastase. The authors concluded that abnormal fecal biomarkers are highly prevalent in patients with IBS symptoms. However, further independent clinical trials are needed on fecal biomarker testing to validate these findings.

In 2017 Dominguez-Munoz et al assessed current evidence in order to compare the utility of functional diagnostic techniques with the fecal elastase-1 (FE-1) test in the following three scenarios: screening for PEI in patients presenting with symptoms suggestive of pancreatic disease, such as abdominal pain or diarrhea; determining the presence of PEI in patients with an established diagnosis of pancreatic disease, such as chronic pancreatitis or cystic fibrosis; determining exocrine status in disorders not commonly tested for PEI, but which have a known association with this disorder. The early diagnosis of pancreatic exocrine insufficiency (PEI) is hindered because many of the functional diagnostic techniques used are expensive and require specialized facilities, which prevent their widespread availability. The authors found that evidence suggests the FE-1 test is reliable for the evaluation of pancreatic function in many pancreatic and non-pancreatic disorders. It is non-invasive, less time-consuming, and unaffected by pancreatic enzyme replacement therapy (PERT). However, FE-1 cannot be considered the gold-standard method for the functional diagnosis of PEI due to its limited sensitivity in mild pancreatic dysfunction and limited specificity in watery stools.

In 2018 Akay et al evaluated the association between fecal elastase levels and Rosemont categories in patients with chronic changes in pancreas detected with endoscopic ultrasound. Seventy patients who were indeterminate of, suggestive of, and consistent with chronic pancreatitis were included in the study. Fifty-four of them were male. Mean age of the patients was 51.7 ± 10.2 year. There were 36 patients in the indeterminate group for chronic pancreatitis. Mean fecal elastase level was 507.1 ± 14.6 μg/g in the indeterminate group. There were 24 patients in the suggestive group of chronic pancreatitis. Mean fecal elastase level was 400.4 ± 121.4 μg/g in the suggestive group of chronic pancreatitis. There were 10 patients, in the consistent group with chronic pancreatitis. Mean fecal elastase level was 134.8 ± 86.1. The difference between the three groups of fecal elastase values was statistically significant compared with Kruskal Wallis test. Ordinal logistic regression analysis showed that there was a significant relation between endosonographic categories and fecal elastase values with Nagelkerke value of 0.704. Conclusions from the study included recommendations for more large-scale, longitudinal studies to demonstrate the relation between endosonographic findings and fecal elastase levels in patients with chronic changes in the pancreas. Also, follow up is needed in those patients who were suggestive of chronic pancreatitis to document pancreas deterioration, along with determining a new cut-off level demonstrating fecal elastase in normal pancreas exocrine function.

In 2022 Johnson et al compared fecal calprotectin and fecal pancreatic elastase assays based on proficiency testing results to understand how results differed across eight calprotectin and five pancreatic elastase manufacturers. Laboratories may have difficulty in switching assays because different manufacturers do not compare well with each other despite having similar reference intervals. Data from proficiency testing performed in Germany (Fecal Diagnostics 01 Survey, INSTAND eV) were investigated. Data were collected from participating laboratories in external quality assessment schemes from 2015 to 2020 for calprotectin and 2017 to 2020 for pancreatic elastase. The manufacturer group mean values and standard deviations were calculated. Reference points were created for each external quality assessment scheme by calculating the average of all manufacturer group means. Deming regression analyses were used to observe the differences across manufacturers. The slopes of the Deming regression spanned 0.37-1.91 for calprotectin and 0.84-1.33 for pancreatic elastase. The calprotectin assays had a high degree of variability in quantitative results by manufacturer. However,

pancreatic elastase assays appear to be harmonized across the different manufacturer when considering the qualitative interpretation. The authors found that both calprotectin and pancreatic elastase assays could be improved by standardization efforts. Also of note, given the clinical utility and data demonstrating high inter-manufacturer variability, calprotectin should be prioritized over pancreatic elastase in standardization efforts.

A 2023 prospective observational study (Holzapfel et al) looked at longitudinal fecal elastase (ELA1) levels in a cohort of preterm infants to determine whether the levels are associated with growth outcomes. Preterm infants are born functionally pancreatic insufficient with decreased pancreatic production of lipase and proteases. Developmental pancreatic insufficiency (PI) may contribute to reduced nutrient absorption and growth failure. This study included 30 infants 24-34 weeks gestational age and birth weight of </=1250 g whom were fed the exclusive human milk diet, consisting of human milk with human milk-based fortifier. ELA1 was quantified by ELISA (enzyme-linked immunosorbent assay) during the first 2 weeks of life [Early; 7.5 +/- 1.8 days of life (DOL)] and after attainment of full, fortified feedings (Late; 63.6 +/- 24.1 DOL). Early ELA1 levels were 192.2 +/- 96.4 microg/g, and Late ELA1 levels were 268.0 +/- 80.3 microg/g, 39.4% higher (P = 0.01). Infants with early PI (ELA1 < 200 microg/g) were more likely male and of lower gestational age, weight, length, and head circumference at birth. These variables, but not PI status, independently predicted somatic growth. The study found that fecal ELA1 in preterm infants fed exclusive human milk diet increases with postnatal age. However, albeit pancreatic function in preterm infants may serve as a biological contributor to early postnatal growth failure, further more robust studies are needed using fecal ELA1 as a predictive biomarker for growth failure to confirm these findings.

Lastly, the American Gastroenterological Association (AGA) in November of 2023 published a Clinical Practice Update on the Epidemiology, Evaluation, and Management of Exocrine Pancreatic Insufficiency: Expert Review on the evaluation and management of pancreatic exocrine insufficiency. Recommendations noted this test is the most appropriate initial test and must be performed on a semi-solid or solid stool specimen and fecal elastase testing can be performed while on pancreatic enzyme replacement therapy. These Best Practice Advice statements were drawn from a review of the published literature and from expert opinion. Because systematic reviews were not performed, these Best Practice Advice statements do not carry formal ratings regarding the quality of evidence or strength of the presented considerations

Malabsorption Evaluation Panel

The Malabsorption Evaluation Panel is used for evaluation of patients with suspected malabsorption, as suggested by chronic diarrhea, unexplained weight loss, or nutritional deficiencies, differentiation between causes of malabsorption, specifically inflammatory conditions, pancreatic insufficiency, and osmotic diarrhea; and detection of protein-losing enteropathy that may be associated with an underlying malabsorption. The panel tests for alpha-1 antitrypsin, calprotectin, pancreatic elastase, and reducing substances. However, there is a lack of evidence regarding the clinical value of this Panel.

Applicable Coding

CPT Codes

Possibly Covered Codes

82653 Elastase, pancreatic (EL-1), fecal; quantitative

82656 Elastase, pancreatic (EL-1), fecal; qualitative or semi-quantitative

Non-Covered Codes

0430U Gastroenterology, malabsorption evaluation of alpha-1-antitrypsin, calprotectin, pancreatic elastase and reducing substances, feces, quantitative

HCPCS Codes

No applicable codes

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advice, care, and treatment. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the member's individual benefit plan that is in effect at the time services are rendered.

The codes for treatments and procedures applicable to this policy are included for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

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