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FEP Medical Policy Manual

FEP 2.04.52 Molecular Testing for the Management of Pancreatic Cysts, Barrett Esophagus, and Solid Pancreaticobiliary Lesions

Effective Policy Date: October 1, 2023

Original Policy Date: June 2012

Related Policies:

None

Molecular Testing for the Management of Pancreatic Cysts, Barrett Esophagus, and Solid Pancreaticobiliary Lesions

Description

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Tests that integrate microscopic analysis with molecular tissue analysis are generally called topographic genotyping. Interpace Diagnostics offers 2 such tests that use the PathFinderTG platform (PancraGEN and BarreGEN). These molecular tests are intended to be used adjunctively when a definitive pathologic diagnosis cannot be made, because of the inadequate specimen or equivocal histologic or cytologic findings, to inform appropriate surveillance or surgical strategies.

OBJECTIVE

The objective of this evidence review is to determine whether testing using topographic genotyping in addition to standard diagnostic or prognostic practices improves the net health outcome in individuals with pancreatic cysts, Barrett esophagus, or solid pancreaticobiliary lesions.

POLICY STATEMENT

Molecular testing using the PathFinderTG system is considered **investigational** for all indications including the evaluation of pancreatic cyst fluid, Barrett esophagus, and solid pancreaticobiliary lesions.

POLICY GUIDELINES

None

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient's existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.

FDA REGULATORY STATUS

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 of the Clinical Laboratory Improvement Amendments. Patented diagnostic test (e.g. PancraGEN) are available only through Interpace Diagnostics (formerly RedPath Integrated Pathology) under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

RATIONALE

Summary of Evidence

For individuals who have pancreatic cysts who do not have a definitive diagnosis after first-line evaluation and who receive standard diagnostic and management practices plus topographic genotyping (PancraGEN molecular testing), the evidence includes retrospective studies of clinical validity and clinical utility. Relevant outcomes are overall survival, disease-specific survival, test validity, change in disease status, morbid events, and quality of life. The best evidence regarding incremental clinical validity comes from the National Pancreatic Cyst Registry report that compared PancraGEN performance characteristics with current international consensus guidelines and provided preliminary but inconclusive evidence of a small incremental benefit for PancraGEN. The analyses from the registry study included only a small proportion of enrolled patients, relatively short follow-up time for observing malignant transformation, and limited data on cases where the PancraGEN results were discordant with international consensus guidelines. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have Barrett esophagus who receive standard prognostic techniques plus topographic genotyping (BarreGEN molecular testing), the evidence includes a systematic review. Relevant outcomes are overall survival, disease-specific survival, test validity, change in disease status, morbid events, and quality of life. The systematic review identified no studies relevant to this evidence review. Two observational studies were excluded based on BCBSA selection criteria because it was unclear whether the test used was specifically BarreGEN or whether the BarreGEN prognostic algorithm was applied for classification. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have solid pancreaticobiliary lesions who do not have a definitive diagnosis after first-line evaluation and who receive standard diagnostic and management practices plus topographic genotyping (PancraGEN molecular testing), the evidence includes 3 observational studies of clinical validity. Relevant outcomes are overall survival, disease-specific survival, test validity, change in disease status, morbid events, and quality of life. Two of the 3 studies had populations with biliary strictures and the other had a population of patients with solid pancreaticobiliary lesions. The studies reported higher sensitivities and specificities when PancraGEN testing was added to cytology results compared with cytology alone. However, the inclusion of patients in the analysis who may not have solid pancreaticobiliary lesions (those with biliary strictures not caused by solid pancreaticobiliary lesions) limits the interpretation of the results. While preliminary results showed a potential incremental benefit for PancraGEN, further research focusing on patients with solid pancreaticobiliary lesions is warranted. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

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

Two (now retired) American Gastroenterological Association (AGA) guidelines previously indicated that "molecular techniques to evaluate pancreatic cysts remain an emerging area of research, and the diagnostic utility of these tests is uncertain"[4], and recommended "against the use of molecular biomarkers to confirm the histological diagnosis of dysplasia or as a method of risk stratification for patients with Barrett's esophagus."[43] As of May 2022, the AGA recommendation on the management of Barrett esophagus is in the process of being updated.

American College of Gastroenterology

In 2022, the American College of Gastroenterology released guidelines on the diagnosis and management of Barrett esophagus.[50] The guidelines stated: "We could not make a recommendation on the use of predictive tools (p53 staining and TissueCypher) in addition to standard histopathology in patients undergoing endoscopic surveillance of BE." The BarreGEN test was not specifically addressed in the guidelines.

In 2018, the American College of Gastroenterology published guidelines on the diagnosis and management of pancreatic cysts.[51] The guidelines stated that the evidence for the use of molecular biomarkers for identifying high-grade dysplasia or pancreatic cancer is insufficient to recommend their routine use. However, molecular markers may help identify intraductal papillary mucinous neoplasms and mucinous cystic neoplasms in cases with an unclear diagnosis and if results are likely to change the management (conditional recommendation; very low quality evidence).

National Comprehensive Cancer Network

National Comprehensive Cancer Network (NCCN) guidelines for pancreatic adenocarcinoma (v.2.2023) recommend that clinicians consider molecular tumor analysis in patients with metastatic disease who are candidates for anti-cancer therapy.[52]

NCCN guidelines for esophageal and esophagogastric junction cancers (v.2.2023)[National Comprehensive Cancer Network (NCCN) do not include recommendations for molecular anatomic pathology or integrated molecular pathology.[53]

U.S. Preventative Services Task Force Recommendations

Not applicable.

Medicare National Coverage

Not applicable.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
June 2012	New policy	
September 2013	Replace policy	Policy updated with literature search; references 4-13, 16 and 17 added. Policy statement unchanged.
September 2014	Replace policy	Policy updated with literature review; References 2-4, 19-23, 30-37 added. Barrett esophagus added to policy statement, which is otherwise unchanged
September 2015	Replace policy	Policy updated with literature review; references 5, 23, and 26- 29 added; reference 21 deleted. The policy statement was revised from not medically necessary to investigational as a correction to align with FDA regulatory status
December 2016	Replace policy	Policy updated with literature review; references 3-4, 8-9, 11, 34, 36-38, 42-44, and 48 added. Tests not commercially available (PathFinderTG Glioma) removed from policy
December 2018	Replace policy	Policy updated with literature review through August 16, 2018; references 50-52 and 54 added. Policy revised with an additional indication - "Individuals with solid pancreaticobiliary lesions who do not have a definitive diagnosis after first line evaluation,. Policy statements unchanged. The title of this policy was changed to "Molecular Testing for the Management of Pancreatic Cysts, Barrett Esophagus, and Solid Pancreaticobiliary Lesions.,
September 2019	Replace policy	Policy updated with literature review through May 29, 2019; references for NCCN updated. Policy statement unchanged.
September 2020	Replace policy	Policy updated with literature review through May 24, 2020. no references added. Policy statement unchanged.
September 2021	Replace policy	Policy updated with literature review through May 25, 2021; no references added, NCCN guidelines updated/ NCCN CNS and hepatobiliary guidelines removed as outside the scope of this policy. Policy statement unchanged.
September 2022	Replace policy	Policy updated with literature review through May 25, 2022; reference added. Policy statements unchanged.
September 2023	Replace policy	Policy updated with literature through May 31, 2023; no references added. Policy statements unchanged.