05-86000-27

Original Effective Date: 07/15/08

Reviewed: 10/24/24

Revised: 11/15/24

Subject: Molecular Testing for the Management of Pancreatic Cysts and Solid Pancreaticobiliary Lesions

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DESCRIPTION:

Topographic genotyping (TG), also called molecular anatomic pathology, integrates microscopic analysis (anatomic pathology) with molecular tissue analysis. Under microscopic examination of tissue and other specimens, areas of interest may be identified and microdissected to increase tumor cell yield for subsequent molecular analysis. Topographic genotyping may permit pathologic diagnosis when first-line analyses are inconclusive.

Interpace Diagnostics has patented a proprietary platform called PathFinderTG®; it provides mutational analyses of patient specimens. The PancraGen™ test, available only through Interpace Diagnostics, uses the PathFinderTG platform. The test is 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.

Summary and Analysis of Evidence: Patients with pancreatic cysts who do not have a definitive diagnosis after first-line evaluation and who receive standard diagnostic and management practices plus topographic genotyping, the evidence includes retrospective studies of clinical validity and clinical utility. 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 the effects of the technology on health outcomes. Patients with 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, the evidence

includes 3 observational studies of clinical validity. 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 the effects of the technology on health outcomes.

POSITION STATEMENT:

Molecular testing using the PathFinderTG® platform (eg, PancraGEN™) is considered **experimental or investigational** for all indications including the evaluation of pancreatic cyst fluid and solid pancreaticobiliary lesions. The evidence is insufficient to determine the effects of the technology on health outcomes.

BILLING/CODING INFORMATION:

There is no specific CPT or HCPCS code for molecular testing using the PathFinderTG platform; unlisted code 81479 or 84999 may be used.

REIMBURSEMENT INFORMATION:

None applicable.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: The following Local Coverage Determination (LCD) was reviewed on the last guideline reviewed date: Loss of Heterozygosity Based Topographic Genotyping with PathfinderTG® (L34864) located at novitas-solutions.com.

DEFINITIONS:

None applicable.

RELATED GUIDELINES:

Tumor/Genetic Markers, 05-86000-22

OTHER:

None applicable.

REFERENCES:

1. Arner DM, Corning BE, et al. Molecular analysis of pancreatic cyst fluid changes clinical management. Endosc Ultrasound. Jan-Feb 2018;7(1):29-33.
2. Blue Cross Blue Shield Association Evidence Positioning System®. 2.04.52 Molecular Testing for the Management of Pancreatic Cysts and Solid Pancreaticobiliary Lesions; 11/24.
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4. Interpace Biosciences®. Molecular Diagnostic Tests; accessed at interpace.com.
5. Khosravi F, Sachdev M, et al. Mutation profiling impacts clinical decision making and outcomes of patients with solid pancreatic lesions indeterminate by cytology. J Pancreas (Online) 2018;19(1):6-11.
6. Kowalski T, Siddiqui A, Loren D, et al. Management of patients with pancreatic cysts: analysis of possible false-negative cases of malignancy. J Clin Gastroenterol. Sep 2016;50(8):649-657.
7. Kushnir VM, Mullady DK, et al. The Diagnostic Yield of Malignancy Comparing Cytology, FISH, and Molecular Analysis of Cell Free Cytology Brush Supernatant in Patients With Biliary Strictures Undergoing Endoscopic Retrograde Cholangiography (ERC): A Prospective Study. J Clin Gastroenterol. Oct 2019; 53(9): 686-692. PMID: 30106834.
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9. Novitas Solutions, Inc. Local Coverage Determination (LCD): Loss of Heterozygosity Based Topographic Genotyping with PathfinderTG® (L34864), accessed at novitas-solutions.com.
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11. Vege SS, Ziring B, et al. American Gastroenterological Association institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. Gastroenterology. Apr 2015;148(4):819-822;quize812-813.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 10/24/24.

GUIDELINE UPDATE INFORMATION:

07/15/08	New Medical Coverage Guideline.
06/15/09	Annual review: position statement maintained, and references updated.
04/15/10	Annual review: position statement maintained, and the description and references updated.
03/15/11	Annual review: position statement maintained and references updated.
03/15/12	Annual review; position statement maintained and references updated.
03/15/13	Annual review; position statement maintained, program exception section and references updated.

03/15/14	Annual review; position statement maintained; Medicare program exception and references updated.
11/01/15	Revision: ICD-9 Codes deleted.
11/15/17	Review; investigational position maintained; title, description section, position statement, and references updated.
12/15/18	Review; investigational status maintained; title, description, position statements, & references updated.
10/15/20	Review; position statement maintained and references updated.
11/15/22	Review: Position statement maintained; references updated.
05/15/24	Position statements maintained; references updated.
10/15/24	Review: Title, position statement, description, and references updated. Refer to policy 05-87000-01 for BarreGEN test.