Protocol

Molecular Testing for the Management of Pancreatic Cysts or Barrett Esophagus

(20452)

(Formerly PathFinderTG® Molecular Testing)

Medical Benefit		**Effective Date**: 10/01/16	**Next Review Date**: 07/19
Preauthorization	No	**Review Dates**: 09/09, 09/10, 07/11, 07/12, 07/13, 07/14, 07/15, 07/16, 07/17, 07/18	

This protocol considers this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With pancreatic cysts who do not have a definitive diagnosis after first-line evaluation	Interventions of interest are: • Standard diagnostic and management practices plus topographic genotyping (PancraGEN molecular testing)	Comparators of interest are: • Standard diagnostic and management practices alone	Relevant outcomes include: • Overall survival • Disease-specific survival • Test accuracy • Test validity • Change in disease status • Morbid events • Quality of life
Individuals: • With Barrett esophagus	Interventions of interest are: • Standard prognostic techniques plus topographic genotyping (BarreGEN molecular testing)	Comparators of interest are: • Standard prognostic techniques alone	Relevant outcomes include: • Overall survival • Disease-specific survival • Test accuracy • Test validity • Change in disease status • Morbid events • Quality of life

DESCRIPTION

Tests that integrate microscopic analysis with molecular tissue analysis are generally called topographic genotyping. Interpace Diagnostics offers two such tests that use the PathFinderTG platform (e.g., PancraGEN, 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.

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 accuracy and 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 the effects of the technology on health outcomes.

For individuals who have Barrett esophagus who receive standard prognostic techniques plus topographic genotyping (BarreGEN molecular testing), the evidence includes two observational studies evaluating the performance characteristics of a panel of genetic markers in Barrett esophagus. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, change in disease status, morbid events, and quality of life. The studies showed that high mutational load could distinguish less from more severe histology and was a predictor of progression in Barrett esophagus. It is not clear whether the test used was specifically BarreGEN or whether the BarreGEN prognostic algorithm was applied for classification. The evidence is insufficient to determine the effects of the technology on health outcomes.

POLICY

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

POLICY GUIDELINES

GENETICS NOMENCLATURE UPDATE

Human Genome Variation Society (HGVS) nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing protocol updates starting in 2017 (see Table PG1). HGVS nomenclature is recommended by HGVS, the Human Variome Project, and the HUman Genome Organization (HUGO). The American College of Medical Genetics and Genomics (ACMG) and Association for Molecular Pathology (AMP) standards and guidelines for interpretation of sequence variants represent expert opinion from ACMG, AMP, and the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology—"pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign"—to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Disease-associated variant	Disease-associated change in the DNA sequence
	Variant	Change in the DNA sequence
	Familial variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives

Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence

Variant Classification	Definition
Likely pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

American College of Medical Genetics and Genomics; AMP: Association for Molecular Pathology

MEDICARE ADVANTAGE

For Medicare Advantage PATHFINDERTG® will be considered **medically necessary** when selectively used as an occasional second-line diagnostic supplement (see Medicare Advantage Policy Guidelines):

- only where there remains clinical uncertainty as to either the current malignancy or the possible malignant potential of the pancreatic cyst based upon a comprehensive first-line evaluation; **AND**
- a decision regarding treatment (e.g., surgery) has NOT already been made based on existing information.

All PATHFINDERTG® indications other than pancreatic cyst fluid evaluation are considered **investigational**.

MEDICARE ADVANTAGE POLICY GUIDELINES

The specific requirements for medical necessity involve:

1. Highly-concise affirmation, documented in the medical record, that a decision regarding treatment has not already been made and that the results of the molecular evaluation will assist in determining if more aggressive treatment than what is being considered is necessary.
2. Previous first-line diagnostics, such as, but not restricted to, the following have demonstrated:
    a. A pancreatic cyst fluid carcinoembryonic antigen (CEA), which is greater than or equal to 200 ng/ml, suggesting a mucinous cyst, but is not diagnostic.
    b. Cyst cytopathologic or radiographic findings, which raise the index of malignancy suspicion, but where second-line molecular diagnostics is expected to be more compelling in the context of a surgical vs. non-surgical care plan.

BACKGROUND

Topographic genotyping, 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.[1]

Interpace Diagnostics has patented a proprietary platform called PathFinderTG; it provides mutational analyses of patient specimens. The patented technology permits analysis of tissue specimens of any size, "including minute needle biopsy specimens," and any age, "including those stored in paraffin for over 30 years."[2] Interpace currently describes in detail one PathFinderTG test called PancraGEN on its website and describes another PathFinder test called BarreGEN as "in the pipeline" (listed and briefly described in Table 1).[3] As stated on the company website, PancraGEN integrates molecular analyses with first-line results (when these are inconclusive) and pathologist interpretation.[4] The manufacturer calls this technique integrated molecular pathology. Test performance information is not provided on the website.

Table 1. PathFinderTG Tests[5]

Test	Description	Specimen Types
PancraGEN	Uses loss of heterozygosity markers, oncogene variants, and DNA content abnormalities to stratify patients according to their risk of progression to cancer	Pancreatobiliary fluid/ERCP brush, pancreatic masses, or pancreatic tissue
PathFinderTG Barrett (now called BarreGEN)	Measures the presence and extent of genomic instability and integrates those results with histology	Esophageal tissue

ERCP: endoscopic retrograde cholangiopancreatography.

MANAGEMENT OF MUCINOUS NEOPLASMS OF THE PANCREAS

True pancreatic cysts are fluid-filled, cell-lined structures, which are most commonly mucinous cysts (intraductal papillary mucinous neoplasm [IPMN] and mucinous cystic neoplasm [MCN]), which are associated with future development of pancreatic cancers. Although mucinous neoplasms associated with cysts may cause symptoms (e.g., pain, pancreatitis), an important reason that such cysts are followed is the risk of malignancy, which is estimated to range from 0.01% at the time of diagnosis to 15% in resected lesions.

Given the rare occurrence but the poor prognosis of pancreatic cancer, there is a need to balance potential early detection of malignancies while avoiding unnecessary surgical resection of cysts. Several guidelines address the management of pancreatic cysts, but high-quality evidence to support these guidelines is not generally available. Although recommendations vary, first-line evaluation usually includes an examination of cyst cytopathologic or radiographic findings and cyst fluid carcinoembryonic antigen. In 2012, an international consensus panel published statements for the management of IPMN and MCN of the pancreas.[6] These statements are referred to as the Fukouka Consensus Guidelines and were based on a symposium held in Japan in 2010, which updated a 2006 publication (Sendai Consensus Guidelines) by this same group.[7] The panel recommended surgical resection for all surgically fit patients with main duct IPMN or MCN. For branch duct IPMN, surgically fit patients with cytology suspicious or positive for malignancy are recommended for surgical resection, but patients without "high-risk stigmata" or "worrisome features" may be observed with surveillance. "High-risk stigmata" are obstructive jaundice in proximal lesions (head of the pancreas); the presence of an enhancing solid component within the cyst; or 10 mm or greater dilation of the main pancreatic duct. "Worrisome features" are pancreatitis; lymphadenopathy; cyst size three cm or greater; thickened or enhancing cyst walls on imaging; five to 10 mm dilation of the main pancreatic duct; or abrupt change in pancreatic duct caliber with distal atrophy of the pancreas.

In 2015, the American Gastroenterological Association published guidelines on the evaluation and management of pancreatic cysts; it recommends patients undergo further evaluation with endoscopic ultrasound-guided fine-needle aspiration only if the cyst has two or more worrisome features (size three cm or larger, a solid component, a dilated main pancreatic duct).[8] The guidelines recommended that patients with a solid component, dilated pancreatic duct, and/or "concerning features" on endoscopic ultrasound-guided fine needle aspiration should undergo surgery.

MANAGEMENT OF BARRETT ESOPHAGUS

Barrett esophagus refers to the replacement of normal esophageal epithelial layer with metaplastic columnar cells in response to chronic acid exposure from gastroesophageal reflux disease. The metaplastic columnar epithelium is a precursor to esophageal adenocarcinoma. These tumors frequently spread before symptoms are present so detection at an early stage might be beneficial. Surveillance for esophageal adenocarcinoma is recommended for those diagnosed with Barrett esophagus.[9] However, there are few data to guide recommendations about management and surveillance, and many issues are controversial. In 2015 guidelines from the American College of Gastroenterology (ACG) and a consensus statement from an international group of experts (Benign Barrett's and CAncer Taskforce [BOB CAT]) regarding management of Barrett esophagus were publish-

ed.[9, 10] ACG recommendations for surveillance are stratified by presence of dysplasia. When no dysplasia is detected, ACG has reported the estimated risk of progression to cancer for patients ranges from 0.2% to 0.5% per year and ACG has recommended endoscopic surveillance every three to five years. For low-grade dysplasia, the estimated risk of progression is about 0.7% per year, and ACG has recommended endoscopic therapy or surveillance every 12 months. For high-grade dysplasia, the estimated risk of progression is about 7% per year, and ACG has recommended endoscopic therapy.[10] The BOB CAT consensus group did not endorse routine surveillance for people with no dysplasia and was unable to agree on surveillance intervals for low-grade dysplasia.[9]

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Patented diagnostic tests (e.g., PancraGEN™) are available only through Interpace Diagnostics (Pittsburgh, PA and New Haven, CT; formerly RedPath Integrated Pathology) under the auspices of CLIA. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. Trikalinos T, Terasawa T, Raman G. A systematic review of loss-of-heterozygosity based topographic genotyping with PathfinderTG®. AHRQ Technology Assessment Program 2010; http://www.cms.gov/determination process/downloads/id68ta.pdf. Accessed March 2015.
2. U.S. Patent #7,014,999. Finkelstein et al. March 21, 2006. Topographic genotyping. http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&p=1&u=%2Fnetahtml%2FPTO%2Fsearchadv.htm&r=16&f=G&l=50&d=PTXT&S1=(redpath+AND+specimen)&OS=redpath+AND+specimen&RS=(redpath+AND+specimen). Accessed April 30, 2015.
3. Interpace Diagnostics. Advancing patient care through molecular diagnostic testing. 2016; http://www.interpacediagnostics.com/. Accessed June 24, 2016.
4. Interpace Diagnostics. How PancraGEN works. 2016; http://www.interpacediagnostics.com/pancragen/howitworks/. Accessed June 24, 2016.
5. RedPath Integrated Pathology. Services. 2013; http://redpathip.com/services/pathfindertg-pancreas. Accessed April 30, 2015.
6. Tanaka M, Fernandez-del Castillo C, Adsay V, et al. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. Pancreatology. May-Jun 2012;12(3):183-197. PMID 22687371

7. Tanaka M, Chari S, Adsay V, et al. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. Pancreatology. 2006;6(1-2):17-32. PMID 16327281
8. Vege SS, Ziring B, Jain R, 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. PMID 25805375
9. Bennett C, Moayyedi P, Corley DA, et al. BOB CAT: a large-scale review and delphi consensus for management of Barrett's Esophagus with no dysplasia, indefinite for, or low-grade dysplasia. Am J Gastroenterol. May 2015;110(5):662-682; quiz 683. PMID 25869390
10. Shaheen NJ, Falk GW, Iyer PG, et al. ACG Clinical Guideline: diagnosis and management of Barrett's esophagus. Am J Gastroenterol. Jan 2016;111(1):30-50; quiz 51. PMID 26526079
11. de Oliveira PB, Puchnick A, Szejnfeld J, et al. Prevalence of incidental pancreatic cysts on 3 tesla magnetic resonance. PLoS One. Mar 23 2015;10(3):e0121317. PMID 25798910
12. Laffan TA, Horton KM, Klein AP, et al. Prevalence of unsuspected pancreatic cysts on MDCT. AJR Am J Roentgenol. Sep 2008;191(3):802-807. PMID 18716113
13. de Jong K, Nio CY, Hermans JJ, et al. High prevalence of pancreatic cysts detected by screening magnetic resonance imaging examinations. Clin Gastroenterol Hepatol. Sep 2010;8(9):806-811. PMID 20621679
14. Gardner TB, Glass LM, Smith KD, et al. Pancreatic cyst prevalence and the risk of mucin-producing adenocarcinoma in US adults. Am J Gastroenterol. Oct 2013;108(10):1546-1550. PMID 24091499
15. Khalid A, Brugge W. ACG practice guidelines for the diagnosis and management of neoplastic pancreatic cysts. Am J Gastroenterol. Oct 2007;102(10):2339-2349. PMID 17764489
16. Oh HC, Kim MH, Hwang CY, et al. Cystic lesions of the pancreas: challenging issues in clinical practice. Am J Gastroenterol. Jan 2008;103(1):229-239; quiz 228, 240. PMID 18076739
17. Scheiman JM, Hwang JH, Moayyedi P. American Gastroenterological Association technical review on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. Gastroenterology. Apr 2015; 148(4):824-848 e822. PMID 25805376
18. Interpace Diagnostics. Clinical utility. 2016; http://www.interpacediagnostics.com/pancragen/clinical-utility/. Accessed June 29, 2016.
19. Al-Haddad MA, Kowalski T, Siddiqui A, et al. Integrated molecular pathology accurately determines the malignant potential of pancreatic cysts. Endoscopy. Feb 2015;47(2):136-142. PMID 25314329
20. Khalid A, McGrath KM, Zahid M, et al. The role of pancreatic cyst fluid molecular analysis in predicting cyst pathology. Clin Gastroenterol Hepatol. Oct 2005;3(10):967-973. PMID 16234041
21. Khalid A, Nodit L, Zahid M, et al. Endoscopic ultrasound fine needle aspirate DNA analysis to differentiate malignant and benign pancreatic masses. Am J Gastroenterol. Nov 2006;101(11):2493-2500. PMID 17029619
22. Khalid A, Pal R, Sasatomi E, et al. Use of microsatellite marker loss of heterozygosity in accurate diagnosis of pancreaticobiliary malignancy from brush cytology samples. Gut. Dec 2004;53(12):1860-1865. PMID 15542529
23. Khalid A, Zahid M, Finkelstein SD, et al. Pancreatic cyst fluid DNA analysis in evaluating pancreatic cysts: a report of the PANDA study. Gastrointest Endosc. May 2009;69(6):1095-1102. PMID 19152896
24. Siddiqui AA, Kowalski TE, Kedika R, et al. EUS-guided pancreatic fluid aspiration for DNA analysis of KRAS and GNAS mutations for the evaluation of pancreatic cystic neoplasia: a pilot study. Gastrointest Endosc. Apr 2013;77(4):669-670. PMID 23498145
25. Schoedel KE, Finkelstein SD, Ohori NP. K-Ras and microsatellite marker analysis of fine-needle aspirates from intraductal papillary mucinous neoplasms of the pancreas. Diagn Cytopathol. Sep 2006;34(9):605-608. PMID 16900481
26. Sawhney MS, Devarajan S, O'Farrel P, et al. Comparison of carcinoembryonic antigen and molecular analysis in pancreatic cyst fluid. Gastrointest Endosc. May 2009;69(6):1106-1110. PMID 19249035

27. Sreenarasimhaiah J, Lara LF, Jazrawi SF, et al. A comparative analysis of pancreas cyst fluid CEA and histology with DNA mutational analysis in the detection of mucin producing or malignant cysts. JOP. Mar 09 2009; 10(2):163-168. PMID 19287110
28. Mertz H. K-ras mutations correlate with atypical cytology and elevated CEA levels in pancreatic cystic neoplasms. Dig Dis Sci. Jul 2011;56(7):2197-2201. PMID 21264513
29. Talar-Wojnarowska R, Pazurek M, Durko L, et al. A comparative analysis of K-ras mutation and carcinoembryonic antigen in pancreatic cyst fluid. Pancreatology. Sep-Oct 2012;12(5):417-420. PMID 23127529
30. Chai SM, Herba K, and Kumarasinghe MP, et al. Optimizing the multimodal approach to pancreatic cyst fluid diagnosis: developing a volume-based triage protocol. Cancer Cytopathol. Feb 2013;121(2):86-100. PMID 22961878
31. Nikiforova MN, Khalid A, Fasanella KE, et al. Integration of KRAS testing in the diagnosis of pancreatic cystic lesions: a clinical experience of 618 pancreatic cysts. Mod Pathol. Nov 2013;26(11):1478-1487. PMID 23743931
32. Lapkus O, Gologan O, Liu Y, et al. Determination of sequential mutation accumulation in pancreas and bile duct brushing cytology. Mod Pathol. Jul 2006;19(7):907-913. PMID 16648872
33. Tamura K, Ohtsuka T, Date K, et al. Distinction of invasive carcinoma derived from intraductal papillary mucinous neoplasms from concomitant ductal adenocarcinoma of the pancreas using molecular biomarkers. Pancreas. Jul 2016;45(6):826-835. PMID 26646266
34. Gillis A, Cipollone I, Cousins G, et al. Does EUS-FNA molecular analysis carry additional value when compared to cytology in the diagnosis of pancreatic cystic neoplasm? A systematic review. HPB (Oxford). May 2015; 17(5):377-386. PMID 25428782
35. Panarelli NC, Sela R, Schreiner AM, et al. Commercial molecular panels are of limited utility in the classification of pancreatic cystic lesions. Am J Surg Pathol. Oct 2012;36(10):1434-1443. PMID 22982886
36. Toll AD, Kowalski T, Loren D, et al. The added value of molecular testing in small pancreatic cysts. JOP. Nov 09 2010;11(6):582-586. PMID 21068490
37. Kung JS, Lopez OA, McCoy EE, et al. Fluid genetic analyses predict the biological behavior of pancreatic cysts: three-year experience. JOP. Sep 2014;15(5):427-432. PMID 25262708
38. Shen J, Brugge WR, Dimaio CJ, et al. Molecular analysis of pancreatic cyst fluid: a comparative analysis with current practice of diagnosis. Cancer. Jun 25 2009;117(3):217-227. PMID 19415731
39. Deftereos G, Finkelstein SD, Jackson SA, et al. The value of mutational profiling of the cytocentrifugation supernatant fluid from fine-needle aspiration of pancreatic solid mass lesions. Mod Pathol. Apr 2014; 27(4):594-601. PMID 24051700
40. Fasanella KE, McGrath KM, Sanders M, et al. Pancreatic endocrine tumor EUS-guided FNA DNA microsatellite loss and mortality. Gastrointest Endosc. May 2009;69(6):1074-1080. PMID 19152901
41. Malhotra N, Jackson SA, Freed LL, et al. The added value of using mutational profiling in addition to cytology in diagnosing aggressive pancreaticobiliary disease: review of clinical cases at a single center. BMC Gastroenterol. Aug 01 2014;14:135. PMID 25084836
42. Winner M, Sethi A, Poneros JM, et al. The role of molecular analysis in the diagnosis and surveillance of pancreatic cystic neoplasms. JOP. Mar 20 2015;16(2):143-149. PMID 25791547
43. RedPath Integrated Pathology. National Pancreatic Cyst Registry. http://www.npcnregistry.com/. Accessed June 28, 2017.
44. Das A, Brugge W, Mishra G, et al. Managing incidental pancreatic cystic neoplasms with integrated molecular pathology is a cost-effective strategy. Endosc Int Open. Oct 2015;3(5):E479-486. PMID 26528505
45. Loren D, Kowalski T, Siddiqui A, et al. Influence of integrated molecular pathology test results on real-world management decisions for patients with pancreatic cysts: analysis of data from a national registry cohort. Diagn Pathol. Jan 20 2016;11(1):5. PMID 26790950
46. 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. PMID 27332745

47. Spechler SJ, Sharma P, Souza RF, et al. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. Gastroenterology. Mar 2011;140(3):1084-1091. PMID 21376940
48. Yantiss RK. Diagnostic challenges in the pathologic evaluation of Barrett esophagus. Arch Pathol Lab Med. Nov 2010;134(11):1589-1600. PMID 21043812
49. Khara HS, Jackson SA, Nair S, et al. Assessment of mutational load in biopsy tissue provides additional information about genomic instability to histological classifications of Barrett's esophagus. J Gastrointest Cancer. Jun 2014;45(2):137-145. PMID 24402860
50. Eluri S, Brugge WR, Daglilar ES, et al. The presence of genetic mutations at key loci predicts progression to esophageal adenocarcinoma in Barrett's esophagus. Am J Gastroenterol. Jun 2015;110(6):828-834. PMID 26010308
51. Spechler SJ, Sharma P, Souza RF, et al. American Gastroenterological Association technical review on the management of Barrett's esophagus. Gastroenterology. Mar 2011;140(3):e18-52; quiz e13. PMID 21376939
52. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: pancreatic adenocarcinoma. Version 2.2017. https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed June 28, 2017.
53. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: central nervous system cancers. Version 1.2016. https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed June 28, 2017.
54. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: esophageal and esophagogastric junction cancers. Version 1.2017. https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed June 28, 2017.
55. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: hepatobiliary cancers. Version 2.2017. https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed June 28, 2017.
56. Novitas Solutions, Inc. (Primary Geographic Jurisdiction - Arkansas, Louisiana, Mississippi, Colorado, New Mexico, Oklahoma, Texas, Delaware, District of Columbia, Maryland, New Jersey, Pennsylvania) Local Coverage Determination (LCD): Loss-of-Heterozygosity Based Topographic Genotyping with PATHFINDERTG® (L34864), Revision Effective Date for services performed on or after 01/04/2016.