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Medical Policy Manual

Topic: PathFinderTG® Molecular Testing

Date of Origin: January 27, 2011

Section: Genetic Testing

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Policy No: 16

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

The PathFinderTG® test (RedPath Integrated Pathology©) is a molecular test used adjunctively in cases for which a definitive pathologic diagnosis cannot be rendered on a tissue or cytology specimen, either due to inadequate specimen or equivocal histologic or cytologic findings.[1] Potential uses described by the manufacturer involve multiple organ systems and clinical scenarios, such as determining reactive versus neoplastic lesions, benign versus malignant lesions, biologically indolent versus aggressive tumors, which premalignant lesions will or will not progress into cancer, whether a synchronous or metachronous tumor represents metastatic spread or a new primary, and expected responses to treatment for various tumors.

The testing involves the following steps:

- Manual microdissection to identify and procure abnormal cells from existing pathology specimens
- DNA extraction and amplification (e.g., polymerase chain reaction [PCR])
- DNA sequencing to identify oncogenic mutations
- Integration of this molecular information with the cytologic or histologic findings provided by the pathologist of record to provide a definitive diagnosis

For some specimens such as fluid aspirates, DNA is extracted from the fluid, since there may be little or no cellular content. The molecular testing consists of applying panels of molecular markers previously defined for each organ system or clinical question.

Some of the tests RedPath offers (e.g., 1p/19q loss, microsatellite instability) are offered by other laboratories as single clinical tests. The remainder of the tests RedPath offers (e.g., KRAS point mutation and loss of heterozygosity [LOH] panels) are typically performed in research settings. The aim of PathFinderTG® testing is to integrate molecular findings into the pathology diagnosis.

This patented diagnostic test is only available through RedPath Integrated Pathology (Pittsburgh, PA). The PathFinderTG® Molecular Test is not subject to review by the U.S. Food and Drug Administration (FDA) because it is a laboratory-developed test (LDT) conducted only at RedPath Integrated Pathology's licensed laboratory. Laboratories performing LDTs must be licensed for high-complexity testing under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). RedPath is licensed under CLIA.

MEDICAL POLICY CRITERIA

Molecular testing using the PathFinderTG® system is considered **investigational** for all indications, including, but not limited to, the evaluation of pancreatic cyst fluid and of suspected or known gliomas.

SCIENTIFIC EVIDENCE

The focus of this review is on evidence related to the ability of test results to:

- Guide decisions in the clinical setting related to either treatment, management, or prevention, and
- Improve health outcomes as a result of those decisions.

Literature Appraisal

- While integrating the molecular information that a test like PathFinderTG® provides is of interest and the subject of research for neoplasms, currently the specific molecular features, associated genetic biomarkers, and their relationships with clinical outcomes are not well defined. Accordingly, their role in clinical decision-making, including selecting treatment options, has not been defined.

- Although the manufacturer cites over 500 papers to support the clinical efficacy of PathFinderTG®, these studies focus on analytical and clinical validity.[2] Collectively, this body of evidence is unreliable due to a number of study limitations, including retrospective design, patient selection bias, lack of investigator blinding, sampling variability of specimens, small sample sizes, lack of adequate follow-up, incomplete follow-up, and lack of validation/replication of findings.

- A systematic review prepared for the Agency for Healthcare Research and Quality (AHRQ) technology assessment program support the above conclusions.[3] Key questions addressed the published evidence on the analytic test performance, diagnostic ability, and clinical validity of the test and what evidence there is comparing the PathFinder test with conventional pathology.

The conclusions were that none of the studies included in the systematic review directly measured whether using loss-of-heterozygosity-based topographic genotyping with PathFinderTG® improved patient-relevant clinical outcomes. The eligible studies on the diagnostic and prognostic ability of the test were small in sample size, had overt methodologic limitations, and all but one performed retrospective assessments. The review noted that the studies did not provide important information on patient selection, patient characteristics, treatments received, clinical end point definitions, justification of sample size, selection of test cutoffs, and selection among various statistical models. In addition, the review noted that there were strong indications that the selection of certain test cutoffs was determined post-hoc, in that the cutoffs varied widely across studies and were not validated in an external population.

- There are no randomized studies in which PathFinderTG® is prospectively compared to existing alternatives and used to direct treatment decisions; therefore it is unknown whether use of this testing improves final health outcomes.

Clinical Practice Guidelines

A search of the U.S. Department of Health & Human Services National Guideline Clearinghouse failed to identify evidence-based clinical practice guidelines that recommend the PathFinderTG test as a method of evaluating pancreatic cyst fluid, suspected or known gliomas, or any other indication.

Summary

There is insufficient evidence to determine whether PathFinderTG molecular testing improves health outcomes for any indication with respect to diagnosis, determining prognosis or predicting response to chemotherapy. Therefore, molecular testing using the PathFinderTG® system is considered investigational for all indications, including but not limited to, the evaluation of pancreatic cyst fluid and of suspected or known gliomas.

REFERENCES

1. BlueCross BlueShield Association Medical Policy Reference Manual "PathFinderTG® Molecular Testing." Policy No. 2.04.52
2. RedPath Integrated Pathology website. [cited 1/18/2011]; Available from: http://www.redpathip.com/publications.asp
3. Trikalinos TA, Terasawa T, Raman G et al. A systematic review of loss-of-heterozygosity based topographic genotyping with PathfinderTG®. AHRQ Technology Assessment Program (Project ID GEND0308). March 2010. [cited 01/18/2011]; Available from: http://www.cms.gov/determinationprocess/downloads/id68ta.pdf

CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	81479	Unlisted molecular pathology procedure

CODES	NUMBER	DESCRIPTION
HCPCS	None	