POLICY STATEMENT:

Based on our criteria and review of the peer-reviewed literature, molecular testing using the Pathfinder TG® system has not been medically proven to be effective and is considered investigational.

Refer to Corporate Medical Policy # 11.01.03 regarding Experimental or Investigational Services.

DESCRIPTION:

The patented PathFinder TG® test is a molecular test to be used adjunctively in cases in 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. This approach may be referred to as “molecular anatomic pathology” or “topographic genotyping”. The PathFinder TG® is described by the manufacturer as a quantitative genetic mutational analysis platform for resolving “indeterminate, atypical, suspicious, equivocal and non-diagnostic specimen” diagnoses from pathology specimens. The manufacturer states that PathFinder TG® focuses on acquired mutational damage rather than inherited genetic predisposition for certain diseases, although there are certain National Institutes of Health (NIH) recommended inherited conditions for which we do test.” The manufacturer states that the temporal sequence of acquired mutational damage revealed by the PathFinder TG® test is an earlier demonstration of tumor biological aggressiveness than current staging systems that rely on the depth of invasion already achieved by the tumor. RedPath, the test provider, suggests that the PathFinder TG® results provide useful and definitive diagnostic and prognostic information and reliably predict treatment response for multiple organ systems. The testing involves the following steps:

I. Manual microdissection to identify and procure abnormal cells from existing pathology specimens;
II. DNA extraction and amplification (e.g., PCR);
III. DNA sequencing to identify oncogenic mutations; and
IV. Integrating 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.

Potential clinical uses described by the company include 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. RedPath proposes that PathFinder TG® is appropriate in clinical practice when the results will alter clinical decision-making. 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 they offer (e.g., KRAS point mutation and loss-of-heterozygosity [LOH] panels) are typically performed in research settings. The aim of PathFinder TG® testing is to integrate molecular findings into the pathology diagnosis.

RATIONALE:

This patented diagnostic test is available only through RedPath Integrated Pathology (Pittsburgh, PA). The PathFinder TG® Molecular Testing 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.

RedPath offers the PathFinder TG® molecular test as a way to provide definitive diagnoses, prognostic information and predict responses to chemotherapy. While integrating the molecular information that a test like PathFinder TG® 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 company claims a wide scope of application for PathFinder TG® in multiple organ systems and clinical scenarios, and lists over 500 papers they reference as “supporting the clinical efficacy of PathFinder TG®,” the most studied applications are for pancreatic cysts and gliomas. Published studies reviewed for this policy include those cited by RedPath as providing “clinical validation” for PathFinder TG®, as well as those representative of the current medical literature describing what is known of the molecular profiles of various tumor types (specifically pancreatic cystic and glial neoplasms) and their potential role in clinical decision-making.

Available published evidence for molecular anatomic pathology (topographic genotyping) focuses on retrospective analyses of pathology specimens examining correlations of test results with tumor characteristics. There are no prospective clinical studies on the use of this analysis in guiding patient management. Current evidence-based guidelines from leading medical professional organizations do not include recommendations for topographic genotyping. Demonstrating utility of a test for diagnostic and prognostic purposes, or to predict therapeutic response requires that results accurately inform clinical decision-making in a manner leading to a net health benefit defined by clinical outcomes. Results must also be clearly reproducible as shown by applying the test (with a priori defined cut-offs) to independent samples for validation. Because the impact of this technology on health outcomes is not known and because outcomes with this technology compared with existing alternatives (i.e., incremental value) are not known, the PathFinder TG® testing is considered investigational.

**CODES:**

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*Eligibility for reimbursement is based upon the benefits set forth in the member’s subscriber contract.*

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

**CPT:**

There are no specific CPT codes for PathFinder TG® analysis

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**HCPCS:**

No specific code.

**ICD9:**

Investigational for all diagnosis codes

**ICD10:**

Investigational for all diagnosis codes

**REFERENCES:**


*Proprietary Information of Excellus Health Plan, Inc.*


KEY WORDS:
Molecular anatomic pathology, PathFinder, RedPath, Topographic genotyping

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**CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS**

According to the Pathfinder TG® website [http://www.redpathip.com/physicians_billing.asp], the test is approved for Medicare reimbursement for all Part-B claims, regardless of patient or physician location. In addition, Pathfinder TG® is covered for Part-A claims in PA, MD, NJ, DE and DC for pancreatic cysts/mass evaluation. All other indications other than pancreatic cyst/mass evaluation were considered investigational and therefore not eligible for coverage due to insufficient data on both analytical and clinical validity.