



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

**Subject Topographic Genotyping
(PathFinderTG® Test)**

Effective Date 10/15/2010
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Coverage Policy Number 0487

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Hyperlink to Related Coverage Policies

Tumor Markers for Diagnosis and Management of Cancer

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

Coverage Policy

CIGNA does not cover topographic genotyping (PathFinderTG® test) for any indication because it is considered experimental, investigational or unproven.

General Background

Topographic genotyping refers to a method of mutational analysis that incorporates minute tumor samples selected according to histopathologic considerations, polymerase chain reaction (PCR) amplification and direct sequencing. The mutational alterations that are found are then correlated with the histology of the tumor. It has been proposed that the results of this testing will provide predictive information that will influence the management of certain cancers. PathFinderTG® (RedPath Integrated Pathology Inc., Pittsburgh, PA) is a patented test that is also referred to as topographic genotyping. PathFinderTG has been proposed as an adjunctive tool to be used when a definitive pathologic diagnosis cannot be determined on tissue or cytology specimen. The inability to obtain a definitive diagnosis using standard methods may be due to an inadequate specimen to equivocal histological or cytological findings. PathFinderTG is purported to provide quantitative genetic mutational analysis of the specimen. The RedPath website notes that the test is "molecular DNA-based cancer diagnostic test which obtains a genetic fingerprint of mutations from routine histology and cytology slides as well as fluid samples."

According to the RedPath website, the PathFinderTG can be utilized to “resolve indeterminate, atypical, suspicious, equivocal and non-diagnostic specimen diagnoses from the original pathology specimen”. The RedPath website notes that PathFinderTG test combines quantitative genetic mutational analysis with pathology in order to differentiate between:

- reactive versus neoplastic lesions
- grade of dysplasia
- benign versus malignant lesions
- metastatic, synchronous and recurrent tumors
- biologically indolent versus aggressive tumors

Proposed applications include cancers of the GI tract, pancreas, head and neck, brain, breast, genito-urinary, and gynecologic tracts. Using a proprietary process, the testing begins with the microdissection of cells from targeted areas of interest from chemically fixed histology and cytology slides. The process is described as incorporating DNA amplification, as well as molecular profiling against a broad panel of mutations (15 to 20 different markers) that include tumor suppressor genes and oncogenes known to be part of the mutational profile for each tumor type.

After the test is performed, the PathFinderTG report is provided to the ordering physician. RedPath describes this as, “a comprehensive description that incorporates the morphologic review with the molecular analysis in a form that is easily understood. A written summary of the number and type of mutations found, if any, is provided and the temporal sequence of mutation acquisition is described. A diagnosis with detailed commentary, including a summary of the molecular profile of the patient’s specimen, is provided in the context of available clinical history and pathology information. “

U.S. Food and Drug Administration (FDA)

No FDA approval was located for PathFinderTG testing. Generally laboratory developed tests are not regulated by the FDA. RedPath Integrated Pathology is accredited by the College of American Pathologists (CAP) Laboratory Accreditation program and has Certificate of Accreditation from Clinical Laboratory Improvement Act of 1988 (CLIA).

Literature Review

A technology assessment and systematic review regarding topographic genotyping with PathFinderTG was commissioned by Centers for Medicare and Medicaid Services (CMS) and conducted by the Tufts Evidence-based Practice Center for the Agency for Healthcare Research and Quality (AHRQ) (Trikalinos TA, et al., 2010). The review included studies evaluating the patented technology, specifically those using loss of heterozygosity (LOH) analysis. LOH is a frequent genetic alteration that is found in many cancers. It is thought that LOH alterations may have prognostic significance. Fifteen studies were included—these pertained to: lung cancer (n=4); pancreatic and biliary tree tumors (n=4); hepatocellular carcinoma (n=4); gliomas, thyroid tumors, lacrimal gland tumors and mucinous tumors of the appendix (n=1 for each). The sample size in the studies ranged from 11 to 103. The review identified no studies regarding the analytic validity of LOH based topographic genotyping with PathFinderTG. The studies were retrospective in design and utilized available archival tissue blocks. One study, molecular profiles of gliomas and reactive gliosis were determined retrospectively and they were used prospectively on 16 diagnostically challenging cases of reactive gliosis versus glial tumors. There were no studies found that evaluated whether the use of LOH based topographic genotyping with PathFinderTG affects patient outcomes. There were no studies identified that compared LOH based topographic genotyping with PathFinderTG with conventional pathology. The review found that “all studies are small, they have important methodological limitations, and they do not address patient-relevant outcomes.”

A prospective multicenter study examined a cohort of 113 patients with pancreatic cysts (Khalid, et al., 2009). Aspirated cyst fluid was examined by PathFinderTG and the results were compared to cytology and pathologic examination of surgically obtained cysts. The study found that the PathFinderTG analysis had 96% specificity in identifying malignant lesions. The cytologic examination missed ten out of 40 malignant lesions, which were correctly identified by PathFinderTG testing. Limitations of the study included limited follow-up, selection bias, lack of investigator blinding to results of DNA analysis.

Studies published regarding topographic genotyping consist mainly of small retrospective studies. Many of these studies do not involve PathFinderTG test. The studies generally focus on the association of the topographic genotyping results with tumor characteristics (Sawhney, et al., 2009; Shen, et al., 2009; Sreenarasimhaiah, et al., 2009; Finkelstein, et al., 2003; Pollack, et al., 2001; Finkelstein, et al., 1998; Riberio, et al., 1998; Kounelis, et al., 1998; Jones, et al., 1997a; Jones, et al., 1997b; Holst, et al., 1997; Pricolo, et al., 1997; Safatle-Ribeiro, et al., 1996; Ribeiro, et al., 1996; Kanbour-shakir, et al., 1996; Finkelstein, et al., 1996; Papadaki, et al., 1996; Przygodzki, et al., 1996; Pricolo, et., 1996; Jacoby, et al., 1995; Finkelstein, et al., 1995).

Studies comparing topographic genotyping with established testing methods are lacking. There do not appear to be prospective studies published in the peer-reviewed medical literature that focus on the clinical validity, the clinical utility of the test or the impact of the test on clinical outcomes.

The RedPath website includes a publication section. Review of this section indicates that generally these articles involve genetic mutational testing of various types of cancers, but do not appear to be specific to the PathFinderTG test and do not allow conclusions to be drawn regarding the clinical utility of the PathFinderTG test.

Professional Societies/Organizations

Review of evidenced-based guidelines from medical professional societies and organizations does not appear to contain the use of topographic genotyping or PathFinderTG in the diagnosis or management of cancer.

Summary

There is insufficient evidence in the published, peer-reviewed, scientific literature to demonstrate that topographic genotyping or the PathFinderTG® (RedPath Integrated Pathology Inc., Pittsburgh, PA) can be used as methods to assist in the diagnosis or management of individuals with cancer when microscopic analysis and staining fail to provide a definitive diagnosis. This testing has not been adequately compared with established testing methods and impact on health outcomes is not known at this time. The clinical utility of topographic genotyping and the PathFinderTG in the diagnosis and management of cancer has not yet been established through well-designed clinical trials.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description
84999 [†]	Unlisted chemistry procedure
89240 [†]	Unlisted miscellaneous pathology test

[†]**Note:** Experimental/Investigational/Unproven/Not Covered when used to report topographic genotyping (PathFinderTG® test).

ICD-9-CM Diagnosis Codes	Description
	All codes

*Current Procedural Terminology (CPT®) © 2010 American Medical Association: Chicago, IL.

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	10/15/2008	0487	Topographic Genotyping (PathFinderTG [®] Test)

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Connecticut General Life Insurance Company has acquired the business of Great-West Healthcare from Great-West Life & Annuity Insurance Company (GWLA). Certain products continue to be provided by GWLA (Life, Accident and Disability, and Excess Loss). GWLA is not licensed to do business in New York. In New York, these products are sold by GWLA’s subsidiary, First Great-West Life & Annuity Insurance Company, White Plains, N.Y.