GUIDELINES
This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder contract. Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards. This guideline is solely for explaining correct procedure reporting and does not imply coverage and reimbursement.

DESCRIPTION
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.

PancraGEN® (Interpace Diagnostics, Parsippany, NJ) (formerly Pathfinder® RedPath Integrated Pathology Inc., Pittsburgh, PA) is a patented test that is also referred to as topographic genotyping. PancraGEN® is performed on the PathfinderTG platform. The test 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. PancraGEN® purportedly assesses the risk of malignancy in patients with pancreatic cysts, providing information for use in management decisions.

There is insufficient evidence in the published, peer-reviewed, scientific literature to demonstrate that topographic genotyping or the PancraGEN® (Interpace Diagnostics, Parsippany, NJ) 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 PancraGEN® in the diagnosis and management of cancer has not yet been established through well-designed clinical trials.

POLICY

<table>
<thead>
<tr>
<th>Topographic genotyping (PancraGEN® Test) for all indications is non-covered for HMO, PPO, Individual Marketplace, &amp; Advantage.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topographic genotyping (PancraGEN® Test) does not require prior authorization for Elite.</td>
</tr>
</tbody>
</table>

HMO, PPO, Individual Marketplace, Advantage
Paramount has determined that topographic genotyping (PancraGEN® Test) is experimental and investigational for all indications and therefore non-covered as there is insufficient data on analytical validity, clinical validity, and clinical utility.

Elite
While there is insufficient evidence in the published medical literature to demonstrate the safety, efficacy and long-term outcomes of topographic genotyping (PancraGEN® Test), per CMS guidelines it is covered for Elite members.

Topographic genotyping (PancraGEN® Test) will be considered medically reasonable and necessary when selectively used as an **occasional second-line diagnostic supplement:**
- 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.

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.

All topographic genotyping (PancraGEN® Test) indications other than pancreatic cyst fluid evaluation are considered investigational and are therefore not considered medically reasonable and necessary due to insufficient data on both analytical and clinical validity.

Specific criteria of non-coverage to include either:
1. Image guided needle aspiration of the pancreatic cyst or cystic component of a mass lesion or dilated duct demonstrate definitive diagnosis of malignancy by cytology; OR
2. Cytology not showing malignancy but meets AGA guidelines to reach a definitive diagnosis of benign disease. Lesions must be:
   a. Under 1 cm
   b. Lack a solid component
   c. Lack concerning cytology features
   d. Lack main pancreatic duct dilatation of > 1 cm in diameter with absence of abrupt change in duct diameter
   e. Have fluid CEA level not exceeding 5 ng/ml

CODING/BILLING INFORMATION
The appearance of a code in this section does not necessarily indicate coverage. Codes that are covered may have selection criteria that must be met. Payment for supplies may be included in payment for other services rendered.

<table>
<thead>
<tr>
<th>CPT CODES</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81479</td>
<td>Unlisted molecular pathology procedure</td>
</tr>
<tr>
<td>84999</td>
<td>Unlisted chemistry procedure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10-CM CODES</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>K86.2</td>
<td>Cyst of pancreas</td>
</tr>
<tr>
<td>K86.3</td>
<td>Pseudocyst of pancreas</td>
</tr>
</tbody>
</table>

TAWG REVIEW DATES: 11/21/2014, 11/12/2015, 11/18/2016, 11/14/2017

REVISION HISTORY EXPLANATION
11/21/14: Added CPT codes 81479 & 84999. Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).
11/12/15: Changed title from Topographic Genotyping (PathFinderTG® Test) to Topographic Genotyping. Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).
11/18/16: Topographic genotyping (PancraGEN® Test) is now covered for Elite per CMS guidelines. Added ICD-10 codes K86.2 & K86.3. Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).
11/14/17: Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG).

REFERENCES/RESOURCES
Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services
Ohio Department of Medicaid http://jfs.ohio.gov/
American Medical Association, Current Procedural Terminology (CPT®) and associated publications and services
Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets
Industry Standard Review
Hayes, Inc.