PTEN Genetic Testing
Policy Number: PG0336
Last Review: 06/26/2019

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.

SCOPE
X Professional
X Facility

DESCRIPTION
The phosphatase and tensin homolog on chromosome 10 (PTEN) is a tumor suppressor gene on chromosome 10q23. The PTEN protein assists with the regulation of cell migration, the adhesion of cells to surrounding tissues, and angiogenesis. Loss of function of this gene contributes to oncogenesis.

Germline mutations in PTEN have been associated with a variety of rare conditions collectively known as PTEN hamartoma tumor syndrome (PHTS). The hallmark clinical feature of PHTS is the presence of hamartomatous tumors, which are benign tumors resulting from an overgrowth of normal tissue. PHTS includes Cowden syndrome (CS), and Bannayan-Riley-Ruvalcaba syndrome (BRRS). Some consider Proteus syndrome (PS) and Proteus-like syndrome to be part of the PHTS spectrum, however, it is now known that AKT1 mutations can cause Proteus syndrome. Although CS is the only PHTS disorder associated with a documented predisposition to multiple malignancies, including breast, thyroid, colon and endometrium, it has been suggested that individuals with other PHTS syndromes associated with PTEN mutations should be assumed to have cancer risks similar to CS. When characteristic features of CS are present, in particular the cancers associated with this condition, but do not meet the strict criteria for a diagnosis of Cowden syndrome, the term "Cowden-like syndrome" (CS-like) is used.

POLICY
**PTEN** gene testing (81321-81323) requires prior authorization.

Multigene panels (including next-generation sequencing [NGS]) for hereditary cancer susceptibility require prior authorization (see medical policy PG0453).

COVERAGE CRITERIA
HMO, PPO, Individual Marketplace, Elite/ProMedica Medicare Plan, Advantage
**PTEN** genetic testing is considered **medically necessary** for the following:
- The individual has a first or second-degree relative with a known **PTEN** mutation (excluding Elite/ProMedica Medicare Plan);
  OR
  - The individual meets clinical diagnostic criteria for and/or has a personal history of:
    o Bannayan-Riley Ruvalcaba syndrome (BRRS)
    o Cowden syndrome/PTEN Hamartoma Tumor Syndrome
  OR
  - The individual has a personal history of:
    o Adult Lhermitte-Duclos disease (cerebellar tumors)
    o Autism spectrum disorder and macrocephaly.
  OR
  - The individual meets any of the following testing criteria for Cowden syndrome:
Two or more biopsy proven trichilemmomas; or
Two or more major criteria (one must be macrocephaly); or
Three or more (without macrocephaly) of the major criteria listed below; or
One major and three or more of the minor criteria listed below; or
Four or more of the minor criteria listed below.

OR
The individual has:
A first-degree relative with a clinical diagnosis of CS or BRRS who is not available for testing, and
One of the major criteria or two of the minor criteria listed below.

Major Criteria
- Breast cancer; or
- Endometrial cancer; or
- Follicular thyroid cancer; or
- Multiple GI hamartomas or ganglioneuromas; or
- Macrocephaly (greater than or equal to the 97th percentile; 58cm in adult women, 60 cm in adult men); or
- Macular pigmentation of glan penis; or
- Mucocutaneous lesions:
  - One biopsy proven trichilemmoma; or
  - Multiple palmoplantar keratoses; or
  - Multiple or extensive oral mucosal papillomatosis; or
  - Multiple cutaneous facial papules (often verrucous).

Minor Criteria
- Autism spectrum disorder; or
- Colon cancer; or
- Esophageal glycogenic acanthosis (≥ 3); or
- Lipomas; or
- Intellectual Disability (i.e., ≤ 75); or
- Papillary or follicular variant of papillary thyroid cancer; or
- Thyroid structural lesions (eg, adenoma, nodule[s], goiter); or
- Renal cell carcinoma; or
- Single GI hamartoma or ganglioneuroma; or
- Testicular lipomatosis; or
- Vascular anomalies (including multiple intracranial developmental venous anomalies).

Note: If two criteria involve the same structure, organ, or tissue, both may be counted as criteria met.

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>
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<tbody>
<tr>
<td>81321 PTEN</td>
<td>(phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis</td>
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<tr>
<td>81322 PTEN</td>
<td>(phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; known familial variant</td>
</tr>
<tr>
<td>81323 PTEN</td>
<td>(phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant</td>
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REVISION HISTORY EXPLANATION
ORIGIINAL EFFECTIVE DATE: 10/22/2015
10/22/15: Policy created to reflect most current clinical evidence per TAWG.
02/26/16: Added effective 1/1/16 new code 81432. Added effective 1/1/16 revised codes 81435, 81436, 81445, 81455. Policy reviewed and updated to reflect most current clinical evidence per TAWG.
10/28/16: Policy reviewed and updated to reflect most current clinical evidence per TAWG.
01/25/18: Removed codes 81432, 81435, 81436, 81445, 81455. Policy reviewed and updated to reflect most current clinical evidence per TAWG.
06/26/2019: Policy reviewed and updated to reflect most current clinical evidence per the National Comprehensive Cancer Network®.
12/21/2020: Medical policy placed on the new Paramount Medical Policy Format

REFERENCES/RESOURCES
Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services
Ohio Department of Medicaid
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.
National Comprehensive Cancer Network® (NCCN), Genetic Familial High-Risk Assessment: Breast and Ovarian, Version 3.2019
Online Mendelian Inheritance of Man (OMIM), Phosphatase and Tensin Homolog, PTEN Genetics Home Reference, National Institute of Health, U.S. Library of Medicine, PTEN gene
Eng, C, GeneReviews®, PTEN Hamartoma Tumor Syndrome