Genetic Testing for PTEN Hamartoma Tumor Syndrome

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Definition

PTEN hamartoma tumor syndrome (PHTS) is an autosomal group of disease conditions caused by a mutation of the PTEN gene on chromosome 10q23 and includes Cowden syndrome (CS), Bannayan-Riley-Ruvalcaba syndrome (BRRS) and Adult Lhermitte-Duclos disease (ALDD). CS is the only PHTS associated with a documented predisposition to cancer, however other PHTS may have cancer risks comparable to CS. The primary clinical manifestation of PHTS is a benign hamartomatous tumor.

Related Medical Guideline

Genetic Counseling and Testing

Guideline

PTEN gene testing is considered medically necessary when **any** of the following criteria are met:

1. 1st or 2nd degree relative has known PTEN mutation
2. Member has personal history of:
    a. Adult Lhermitte-Duclos disease (ALDD)
    b. Bannayan RIley-Ruvalcaba syndrome (BRRS)
    c. Autism spectrum disorder and macrocephaly
    d. Proteus Syndrome (hamartomatous overgrowth of multiple tissues, as well as connective tissue nevi and hyperostoses)
3. Member meets any of the following criteria for Cowden/PHTS syndrome:
    a. At least 2 biopsy proven trichilemmomas
    b. Macrocephaly plus ≥ 1 of the other major criteria
    c. ≥ 3 major criteria without macrocephaly
    d. 2 major and ≥ 2 of the minor criteria
    e. 1 major and ≥ 3 minor criteria
    f. ≥ 4 minor criteria

4. Member has a family history of both of the following:
    a. At-risk relative with a clinical diagnosis of CS/PHTS or BRRS and no previous genetic testing
    b. At-risk relative has 1 major criteria or 2 minor criteria

Major and Minor Criteria for PTEN Genetic Testing

Major	Minor
Breast cancer	Autism spectrum disorder (without macrocephaly)
Follicular thyroid cancer	Mental retardation (IQ < 75)
Endometrial cancer	Papillary thyroid cancer (papillary or follicular)
Multiple GI hamartomas or ganglioneuromas	Thyroid structural lesions (e.g., adenoma, nodule(s), goiter)
Macrocephaly (≥ 97th percentile; 58 cm in adult women, 60 cm in adult men)	Colon cancer
Mucocutaneous lesions	Renal cell carcinoma
One biopsy-proven trichilemmoma	Single gastrointestinal hamartoma or ganglioneuroma
Multiple palmoplantar keratoses	Esophageal glycogenic acanthoses (≥ 3)
Multiple or extensive oral mucosal papillomatosis	Lipomas
Multiple cutaneous facial papules (often verrucous)	Testicular lipomatosis
Macular pigmentation of glans penis	Vascular anomalies (including multiple intracranial developmental venous anomalies)
≥ 3 mucocutaneous neuromas	

Limitations/Exclusions

PTEN gene testing is considered experimental and investigational for all other conditions that do not meet the above criteria

Applicable Procedure Codes

81321	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis
81322	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; known familial variant
81323	PTEN (phosphatase and tensin homolog) (e.g., Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant

References

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3. National Comprehensive Cancer Network (NCCN). NCCN guidelines Genetic/Familial High Risk Assessment: Breast, Ovarian, and Pancreatic. V1.2022. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf. Accessed December 16, 2021.
4. Pilarski R, Burt R, Kohlman W, et al. Cowden syndrome and the PTEN hamartoma tumor syndrome: systematic review and revised diagnostic criteria. J Natl Cancer Inst. 2013; 105(21):1607-1616.

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