

## Clinical criteria for the diagnosis of PTEN hamartoma tumor syndrome

(Pilarski R. et al., *J Natl Cancer Inst.* 2013;105(21):1607-16)

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### Major criteria

- Breast cancer
- Endometrial cancer (epithelial)
- Thyroid cancer (follicular)
- Gastrointestinal hamartomas (including ganglioneuromas, but excluding hyperplastic polyps;  $\geq 3$ )
- Lhermitte-Duclos disease (adult)
- Macrocephaly ( $\geq 97$  percentile: 58 cm for females, 60 cm for males)
- Macular pigmentation of the glans penis
- Multiple mucocutaneous lesions (any of the following):
  - Multiple trichilemmomas ( $\geq 3$ , at least one biopsy proven)
  - Acral keratoses ( $\geq 3$  palmoplantar keratotic pits and/or acral hyperkeratotic papules)
  - Mucocutaneous neuromas ( $\geq 3$ )
  - Oral papillomas (particularly on tongue and gingiva), multiple ( $\geq 3$ ) OR biopsy proven OR dermatologist diagnosed

### Minor criteria

- Autism spectrum disorder
- Colon cancer
- Esophageal glycogenic acanthosis ( $\geq 3$ )
- Lipomas ( $\geq 3$ )
- Mental retardation ( $\text{IQ} \leq 75$ )
- Renal cell carcinoma
- Testicular lipomatosis
- Thyroid cancer (papillary or follicular variant of papillary)
- Thyroid structural lesions (eg, adenoma, multinodular goiter)
- Vascular anomalies (including multiple intracranial developmental venous anomalies)

### **Diagnostic criteria interpretation**

#### In an individual:

- Three or more major criteria, but one must include macrocephaly, Lhermitte-Duclos disease or gastrointestinal hamartomas
- OR
- Two major and three minor criteria

#### In a family where one individual meets revised PTEN hamartoma tumor syndrome diagnostic criteria or has a PTEN mutation:

- Any two major criteria with or without minor criteria
- OR
- One major criteria and two minor criteria
- OR
- Three minor criteria