The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000314.8(PTEN):c.157G>A (p.Val53Ile)

Version: 1.0

CA211469780

2136907 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: c1e8d037-62a8-452a-9b2c-47bc65cddb25
Approved on: 2026/6/17
Published on: 2026/6/24

HGVS expressions

NM_000314.8:c.157G>A
NM_000314.8(PTEN):c.157G>A (p.Val53Ile)
NC_000010.11:g.87894102G>A
CM000672.2:g.87894102G>A
NC_000010.10:g.89653859G>A
CM000672.1:g.89653859G>A
NC_000010.9:g.89643839G>A
NG_007466.2:g.35664G>A
ENST00000700029.2:c.157G>A
ENST00000710265.1:c.157G>A
ENST00000472832.3:c.157G>A
ENST00000688158.2:n.899+13664G>A
ENST00000688922.2:c.157G>A
ENST00000700021.1:c.157G>A
ENST00000700022.1:c.157G>A
ENST00000706954.1:c.157G>A
ENST00000706955.1:c.*192G>A
ENST00000686459.1:c.157G>A
ENST00000688158.1:c.*275+13664G>A
ENST00000688308.1:c.157G>A
ENST00000688922.1:c.26G>A
ENST00000693560.1:c.676G>A
ENST00000371953.8:c.157G>A
ENST00000371953.7:c.157G>A
ENST00000462694.1:n.159G>A
ENST00000610634.1:c.55G>A
NM_000314.5:c.157G>A
NM_000314.6:c.157G>A
NM_001304717.2:c.676G>A
NM_001304718.1:c.-549G>A
NM_000314.7:c.157G>A
NM_001304717.5:c.676G>A
NM_001304718.2:c.-549G>A

Met criteria codes 5

Expert Panel

Pathogenic

PS2 PP2 PP3 PM6_Strong PM2_Supporting

Not Met criteria codes 1

PS4

Evidence Links 1

PTEN VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen PTEN Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PTEN Version 3.2.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

PTEN VCEP

PTEN c.157G>A (p.Val53Ile or NC_000010.10:g.89653859G>A) meets criteria to be classified as Pathogenic for PTEN Hamartoma Tumor syndrome in an autosomal dominant manner using modified ACMG criteria (ACMG Classification Rules Specified for PTEN Variant Curation version 3.1.0). Please see a summary of the rules and criteria codes in the "PTEN ACMG Specifications Summary" document (assertion method column). PM6_S: One proband with presumed de novo occurrence (maternity/paternity not confirmed) for a patient with highly specific phenotype. (internal laboratory contributor(s)). PS2: De novo (both maternity and paternity confirmed) observation in a patient with the disease and no family history (internal laboratory contributor(s)). PP2: PTEN is defined by the PTEN Expert Panel as a gene that has a low rate of benign missense variation and where missense variants are a common mechanism of disease. PP3: REVEL score > 0.7 (score of this variant =0.75) PM2_P: Absent in large sequenced populations OR present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. (PMID 27535533).

Met criteria codes

PS2	✔	De novo (both maternity and paternity confirmed) observation in a patient with the disease and no family history. (internal laboratory contributor(s)) GeneDx #3: exome trio, de novo (parentage confirmed) in a M child with autism and developmental delays, no OFC measure or other info provided.
PP2	✔	PTEN is defined by the PTEN Expert Panel as a gene that has a low rate of benign missense variation and where missense variants are a common mechanism of disease.
PP3	✔	REVEL score > 0.7 (score of this variant =0.75)
PM6_Strong	✔	One proband with presumed de novo occurrence (maternity/paternity not confirmed) for a patient with highly specific phenotype. (internal laboratory contributor(s)) Gene Dx #1: Single gene testing, de novo (parents just with targeted variant testing, assumed) in a 1yo M with extreme macrocephaly (+4SD) and global developmental delay.
PM2_Supporting	✔	Absent in large sequenced populations OR present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. (PMID 27535533). Absent in large sequenced populations OR present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. PubMed:27535533

Not Met criteria codes

PS4		✖	Gene Dx #2: cancer panel, adult F with breast cancer, colon polyps, and leukemia. No weight added. Adult proband with: Macrocephaly (61 cm) (+6 CC score, sex is unknown to asses from extreme macrocephaly), Breast Fibrocystic Disease (+1 CC score), Ductal Breast Carcinoma (age 39 years) (+4 CC score), Intraductal Papilloma of Breast, Malignant Neoplasm of Skin (unknown type), Pulmonary Nodule (Cleveland Clinic, PMID: 25669429). Total CC score = 11, no weight added.

Curation History

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