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.408T>G (p.Cys136Trp)

Version: 1.0

CA357779

224543 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: a8ec82c1-a3b5-4e8c-ad81-ac59b2b541ef
Approved on: 2025/4/4
Published on: 2025/6/5

HGVS expressions

NM_000314.8:c.408T>G
NM_000314.8(PTEN):c.408T>G (p.Cys136Trp)
NC_000010.11:g.87933167T>G
CM000672.2:g.87933167T>G
NC_000010.10:g.89692924T>G
CM000672.1:g.89692924T>G
NC_000010.9:g.89682904T>G
NG_007466.2:g.74729T>G
ENST00000700029.2:c.408T>G
ENST00000710265.1:c.408T>G
ENST00000472832.3:c.408T>G
ENST00000688158.2:n.1143T>G
ENST00000688922.2:c.*238T>G
ENST00000700021.1:c.363T>G
ENST00000700022.1:c.408T>G
ENST00000700029.1:c.242T>G
ENST00000706954.1:c.408T>G
ENST00000706955.1:c.*443T>G
ENST00000686459.1:c.408T>G
ENST00000688158.1:c.*519T>G
ENST00000688308.1:c.408T>G
ENST00000688922.1:c.329T>G
ENST00000693560.1:c.927T>G
ENST00000371953.8:c.408T>G
ENST00000371953.7:c.408T>G
ENST00000498703.1:n.234T>G
ENST00000610634.1:c.306T>G
NM_000314.5:c.408T>G
NM_000314.6:c.408T>G
NM_001304717.2:c.927T>G
NM_001304718.1:c.-343T>G
NM_000314.7:c.408T>G
NM_001304717.5:c.927T>G
NM_001304718.2:c.-343T>G

Pathogenic

Met criteria codes 6

PS3_Moderate PM6_Strong PM2_Supporting PM5 PP2 PP3

Not Met criteria codes 1

PS4

Evidence Links 0

Expert Panel

PTEN VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen PTEN Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PTEN Version 3.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

PTEN VCEP

PTEN c.408T>G (p.Cys136Trp) meets criteria to be classified as pathogenic for PTEN Hamartoma Tumor syndrome in an autosomal dominant manner using modified ACMG criteria (PMID 30311380). Please see a summary of the rules and criteria codes in the "PTEN ACMG Specifications Summary" document (assertion method column). PM6_S: Assumed de novo, but without confirmation of paternity and maternity in a patient with the disease and no family history (internal laboratory contributor(s) SCV003926429.1). PM5: Missense change at an amino acid residue where a different missense change determined to be pathogenic or likely pathogenic and with equal or lesser BLOSUM62 score has been seen before (ClinVar Variation ID 189406, SCV000840468.3). PS3_M: Functional studies supportive of a damaging effect on the gene or gene product. Score of this variant = -3.54 (≤ -1.11) on a high throughput phosphatase assay (PMID 29706350). PP3: REVEL score > 0.7 (score of this variant = 0.954). 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. PM2_P: Absent in large sequenced populations (PMID 27535533).

Met criteria codes

PS3_Moderate	✔	Mighell et al 2018 (PMID 29706350)
PM6_Strong	✔	GeneDx proband (ped score = 7)
PM2_Supporting	✔	Absent in gnomAD v2 and v4
PM5	✔	BLOSUM score for focal variant (-2) is the same as one candidate classified as P y the VCEP (c.407G>A p.Cys136Tyr)
PP2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✔	REVEL score (0.954) > 0.7

Not Met criteria codes

PS4	✖	Ambry proband: 0.5 proband points

Curation History

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