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_000314.6(PTEN):c.477G>T (p.Arg159Ser)

Version: 3.0

CA16602438

375959 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 6ba47371-001e-4be9-8252-885e7e1a5f99
Approved on: 2025/12/5
Published on: 2025/12/17

HGVS expressions

NM_000314.6(PTEN):c.477G>T (p.Arg159Ser)
NM_000314.6:c.477G>T
NC_000010.11:g.87933236G>T
CM000672.2:g.87933236G>T
NC_000010.10:g.89692993G>T
CM000672.1:g.89692993G>T
NC_000010.9:g.89682973G>T
NG_007466.2:g.74798G>T
ENST00000700029.2:c.477G>T
ENST00000710265.1:c.477G>T
ENST00000472832.3:c.477G>T
ENST00000688158.2:n.1212G>T
ENST00000688922.2:c.*307G>T
ENST00000700021.1:c.432G>T
ENST00000700022.1:c.477G>T
ENST00000700029.1:c.311G>T
ENST00000706954.1:c.477G>T
ENST00000706955.1:c.*512G>T
ENST00000686459.1:c.477G>T
ENST00000688158.1:c.*588G>T
ENST00000688308.1:c.477G>T
ENST00000688922.1:c.398G>T
ENST00000693560.1:c.996G>T
ENST00000371953.8:c.477G>T
ENST00000371953.7:c.477G>T
ENST00000498703.1:n.303G>T
ENST00000610634.1:c.375G>T
NM_000314.5:c.477G>T
NM_001304717.2:c.996G>T
NM_001304718.1:c.-274G>T
NM_000314.7:c.477G>T
NM_001304717.5:c.996G>T
NM_001304718.2:c.-274G>T
NM_000314.8:c.477G>T

Likely Pathogenic

Met criteria codes 5

PM2_Supporting PP2 PP3 PM5 PS3_Moderate

Not Met criteria codes 21

PP1 PP4 BA1 PM6 PVS1 PM1 PM3 PM4 BS2 BS1 BS4 BS3 PS1 PS2 PS4 BP5 BP7 BP4 BP3 BP1 BP2

Evidence Links 2

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.477G>T (p.Arg159Ser) meets criteria to be classified as likely 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). PS3: Phosphatase activity <50% of wild type (PMID 29706350) PM2: Absent in large sequenced populations (PMID 27535533). 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. PM5: the VCEP has classified p.R159K as PATH, it has a higher BLOSUM score

Met criteria codes

PM2_Supporting	✔	absent gnomAD
PP2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✔	REVEL score of 0.98
PM5	✔	the VCEP has classified p.R159K as PATH, it has a higher BLOSUM score
PS3_Moderate	✔	Phosphatase score -3.65, truncation-like range. PubMed:29706350 Article studied variant for splicing impact. Identified in TCGA tumor; RT-PCR showed 21bp deletion. However, fig. 5 mini-gene appears same as WT? No apparent impact on native site, but possible strengthening of alternative SDS. PubMed:29617666

Not Met criteria codes

PP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4	✖	

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BA1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BP7		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

Showing 1 to 5 of 5 rows

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