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.424C>T (p.Arg142Trp)

Version: 1.1

CA000455

197662 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 91dab46a-c7bf-4a39-b7ee-9ca9cefa19c5
Approved on: 2026/6/16
Published on: 2026/6/26

HGVS expressions

NM_000314.8:c.424C>T
NM_000314.8(PTEN):c.424C>T (p.Arg142Trp)
NC_000010.11:g.87933183C>T
CM000672.2:g.87933183C>T
NC_000010.10:g.89692940C>T
CM000672.1:g.89692940C>T
NC_000010.9:g.89682920C>T
NG_007466.2:g.74745C>T
ENST00000700029.2:c.424C>T
ENST00000710265.1:c.424C>T
ENST00000472832.3:c.424C>T
ENST00000688158.2:n.1159C>T
ENST00000688922.2:c.*254C>T
ENST00000700021.1:c.379C>T
ENST00000700022.1:c.424C>T
ENST00000700029.1:c.258C>T
ENST00000706954.1:c.424C>T
ENST00000706955.1:c.*459C>T
ENST00000686459.1:c.424C>T
ENST00000688158.1:c.*535C>T
ENST00000688308.1:c.424C>T
ENST00000688922.1:c.345C>T
ENST00000693560.1:c.943C>T
ENST00000371953.8:c.424C>T
ENST00000371953.7:c.424C>T
ENST00000498703.1:n.250C>T
ENST00000610634.1:c.322C>T
NM_000314.5:c.424C>T
NM_000314.6:c.424C>T
NM_001304717.2:c.943C>T
NM_001304718.1:c.-327C>T
NM_000314.7:c.424C>T
NM_001304717.5:c.943C>T
NM_001304718.2:c.-327C>T

Uncertain Significance

Met criteria codes 4

PP2 PP3 BS3_Supporting PM2_Supporting

Not Met criteria codes 7

PS1 PS3 BA1 PM5 BS1 BP4 BP1

Evidence Links 1

Expert Panel

PTEN VCEP

Criteria Specification Information

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

Evidence submitted by expert panel

PTEN VCEP

NM_000314.8(PTEN):c.424C>T (p.Arg142Trp) is currently classified as a variant of uncertain significance 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). BS3_P: Well-established functional studies show no deleterious effect: Phosphatase activity >0 (score of this variant = 0.45) per Mighell et al. 2018 (PMID: 29706350). 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 = 0.716). PM2_P: Absent in gnomAD. Although this variant has been observed de novo in published literature (PMID 38335860) and internal laboratory cases, many of these patients and several others did not have features consistent with PTEN Hamartoma Tumor syndrome (PMID 26534844). This variant occurs as a CpG dinucleotide site; such sites have an increased rate of spontaneous deamination leading to de novo mutation (PMID 16570853). We believe that de novo observations of this variant are most likely incidental findings due to the hypermutable nature of this nucleotide position, and are not awarding de novo criteria as evidence towards pathogenicity given the inconsistent phenotypes present.

Met criteria codes

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 = 0.716).
BS3_Supporting	✔	Well-established functional studies show no deleterious effect: Phosphatase activity >0 (score of this variant = 0.45) per Mighell et al. 2018 (PMID: 29706350). Phosphatase activity >0 (score of this variant = 0.45) PubMed:29706350
PM2_Supporting	✔	gnomAD v2 (10-89692940-C-T): 1 total allele (AF in Total Pop 0.0003978% < 0.001%) gnomAD v4 (10-87933183-C-T): 5 total alleles. 5/1179810 NFE alleles (SubPop AF 0.0004238% < 0.002%)

Not Met criteria codes

PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PS3	✖	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
PM5	✖	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
BP4	✖	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

Curation History

Showing 1 to 2 of 2 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000314.8(PTEN):c.424C>T (p.Arg1...	Uncertain Significance	PTEN Hamartoma Tumor Syndrome	2026-06-26	1.1	ClinGen PTEN Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PTEN Version 3.2.0	PTEN
View	NM_000314.8(PTEN):c.424C>T (p.Arg1...	Uncertain Significance	PTEN Hamartoma Tumor Syndrome	2024-05-17	1.0	ClinGen PTEN Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PTEN Version 3.1.0	PTEN

Showing 1 to 2 of 2 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.