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.44G>C (p.Arg15Thr)*

Version: 1.0

*CA377781931*

*428243 (ClinVar)*

**Gene**: PTEN (HGNC:5728)
**Condition**: PTEN hamartoma tumor syndrome (MONDO:0017623)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** c0525249-345f-416d-89cd-fa8b4de862c3
**Approved on**: 2023/8/4
**Published on**: 2023/10/19

## *HGVS expressions*

**NM_000314.8:c.44G>C**
**NM_000314.8(PTEN):c.44G>C (p.Arg15Thr)**
NC_000010.11:g.87864513G>C
CM000672.2:g.87864513G>C
NC_000010.10:g.89624270G>C
CM000672.1:g.89624270G>C
NC_000010.9:g.89614250G>C
NG_007466.2:g.6075G>C
NG_033079.1:g.3925C>G
ENST00000700029.2:c.44G>C
ENST00000710265.1:c.44G>C
ENST00000472832.3:c.44G>C
ENST00000688922.2:c.44G>C
ENST00000700021.1:c.44G>C
ENST00000700022.1:c.44G>C
ENST00000706954.1:c.44G>C
ENST00000706955.1:c.44G>C
ENST00000686459.1:c.44G>C
ENST00000688158.1:c.44G>C
ENST00000688308.1:c.44G>C
ENST00000693560.1:c.563G>C
ENST00000371953.8:c.44G>C
ENST00000371953.7:c.44G>C
ENST00000462694.1:n.46G>C
ENST00000487939.1:n.65G>C
ENST00000610634.1:c.-59G>C
ENST00000618586.1:n.13G>C
NM_000314.5:c.44G>C
NM_000314.6:c.44G>C
NM_001304717.2:c.563G>C
NM_001304718.1:c.-662G>C
NM_000314.7:c.44G>C
NM_001304717.5:c.563G>C
NM_001304718.2:c.-662G>C

**Likely Pathogenic**

**Met criteria codes** 5

PS3_Moderate PM2_Supporting PS2 PP2 PP3

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 3.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***PTEN VCEP***

**NM_000314.8(PTEN):c.44G>C (p.Arg15Thr) meets criteria to be classified as likely pathogenic for PTEN Hamartoma Tumor syndrome in an autosomal dominant manner using modified ACMG criteria (ACMG Classification Rules Specified for PTEN Variant Curation version 3.0.0). Please see a summary of the rules and criteria codes in the "PTEN ACMG Specifications Summary" document (assertion method column). PS2: De novo (both maternity and paternity confirmed) observation in a patient with the disease and no family history. [internal laboratory contributor(s)] PS3_M: Functional studies showing a damaging effect on protein function. Phosphatase activity ≤ -1.11 per Mighell et al. 2018 (PMID: 29706350). This variant: score of -1.2. PM2_Supporting: Absent in large sequenced populations OR present at extremely low (<0.00001, 0.001%) allele frequency in the gnomAD cohort. (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. PP3: in silico REVEL score of 0.87 (>0.7)**

**Met criteria codes**

| | | |
|---|---|---|
| **PS3_Moderate** | ✔ | Mighell et al. 2018 PMID: 29706350 Lipid phosphatase activity score in the hypomorphic range, -1.2 (TRUE). |
| **PM2_Supporting** | ✔ | Absent in gnomAD |
| **PS2** | ✔ | Confirmed de novo case from Invitae. Patient (child) with macrocephaly, thickened corpus callosum, mild asymmetry, and autism with mild delay. Paternity/maternity were confirmed. Peds score of 4 (internal laboratory contributor). |
| **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** | ✔ | in silico REVEL score of 0.87 (>0.7) |

Curation History

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