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.599T>C (p.Phe200Ser)

Version: 2.0

CA000532

189414 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 633ec420-0afb-4647-b05d-ed0a118f2469
Approved on: 2025/12/5
Published on: 2025/12/17

HGVS expressions

NM_000314.8:c.599T>C
NM_000314.8(PTEN):c.599T>C (p.Phe200Ser)
NC_000010.11:g.87952224T>C
CM000672.2:g.87952224T>C
NC_000010.10:g.89711981T>C
CM000672.1:g.89711981T>C
NC_000010.9:g.89701961T>C
NG_007466.2:g.93786T>C
ENST00000700029.2:c.599T>C
ENST00000710265.1:c.599T>C
ENST00000472832.3:c.599T>C
ENST00000688158.2:n.1334T>C
ENST00000688922.2:c.*429T>C
ENST00000700021.1:c.554T>C
ENST00000700022.1:c.493-5629T>C
ENST00000700023.1:n.1757T>C
ENST00000700024.1:n.1991T>C
ENST00000700025.1:n.1368T>C
ENST00000700029.1:c.433T>C
ENST00000706954.1:c.599T>C
ENST00000706955.1:c.*634T>C
ENST00000686459.1:c.*185T>C
ENST00000688158.1:c.*710T>C
ENST00000688308.1:c.599T>C
ENST00000688922.1:c.520T>C
ENST00000693560.1:c.1118T>C
ENST00000371953.8:c.599T>C
ENST00000371953.7:c.599T>C
ENST00000472832.2:c.26T>C
NM_000314.5:c.599T>C
NM_000314.6:c.599T>C
NM_001304717.2:c.1118T>C
NM_001304718.1:c.8T>C
NM_000314.7:c.599T>C
NM_001304717.5:c.1118T>C
NM_001304718.2:c.8T>C

Likely Pathogenic

Met criteria codes 4

PM2 PS4_Moderate PP2 PP3

Not Met criteria codes 22

PVS1 BS2 BS1 BS4 BS3
BP5 BP7 BP4 BP3 BP1 BP2
PM6 PM1 PM3 PM5 PM4
PS1 PS2 PS3 BA1 PP1 PP4

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 3.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

PTEN VCEP

PTEN c.599T>C (p.Phe200Ser) 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). PM2_P: Absent in gnomad v4. PS4_M: Probands with phenotype specificity score of 2-3.5. (internal laboratory contributor SCV000222124.11) 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 of 0.857, > 0.7 threshold.

Met criteria codes

PM2	✔	Variant absent gnomAD v4.
PS4_Moderate	✔	GDX1: child with extreme macrocephaly, DD, other neuro features, peds score = 5 = 1 PS4 point. GDX2: child with non-extreme macrocephaly, dev delay, lipoma vs. AVM, hemangioma, peds score minimum = 6 = 1 PS4 point. GDX3: child with autism, inherited from father, no other information available. No weight added.
PP2	✔	PTEN is a gene that has a low rate of benign missense variation and where missense variants are a common mechanism of disease.
PP3	✔	REVEL score of 0.857, > 0.7 threshold.

Not Met criteria codes

PVS1	✖	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	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3	ℹ	✖	Score -3.25 BUT not high confidence - no criteria can apply. **PubMed:29706350**
BP5	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	ℹ	✖	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	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1	ℹ	✖	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
PM5	ℹ	✖	Phe200Val at same codon, no VCEP curation, cannot apply PM5.
PM4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PS3		✖	Low confidence for cummulative functional score in Mighell et al. 2018 (PMID: 29706350). Score -3.25 BUT not high confidence - no criteria can apply. PubMed:29706350
BA1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1		✖	GDX1/Invitae/Eng lab shared family: variant present in proband with macrocephaly, dev delay, penile freck; father with macrocephaly, lipomas, hemangioma, oral papillomas, polyps and pat uncle with lipomas and polyps. Also unaffected PGM and her mother with breast cancer dx 80. Per VCEP review count 2 meioses (proband, dad, pat uncle).
PP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

Showing 1 to 3 of 3 rows

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