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.752G>T (p.Gly251Val)

Version: 1.0

CA377484997

536548 (ClinVar)

Gene: PTEN (HGNC:5728)
Condition: PTEN hamartoma tumor syndrome (MONDO:0017623)
Inheritance Mode: Autosomal dominant inheritance
UUID: 93b161cc-a3f6-4dd0-8b7b-3e0e31efe08a
Approved on: 2025/4/4
Published on: 2025/6/5

HGVS expressions

NM_000314.8:c.752G>T
NM_000314.8(PTEN):c.752G>T (p.Gly251Val)
NC_000010.11:g.87957970G>T
CM000672.2:g.87957970G>T
NC_000010.10:g.89717727G>T
CM000672.1:g.89717727G>T
NC_000010.9:g.89707707G>T
NG_007466.2:g.99532G>T
ENST00000700029.2:c.752G>T
ENST00000710265.1:c.752G>T
ENST00000472832.3:c.752G>T
ENST00000688158.2:n.1487G>T
ENST00000688922.2:c.*582G>T
ENST00000700021.1:c.707G>T
ENST00000700022.1:c.*91G>T
ENST00000700023.1:n.1910G>T
ENST00000700024.1:n.2144G>T
ENST00000700025.1:n.1521G>T
ENST00000700026.1:n.389G>T
ENST00000700029.1:c.586G>T
ENST00000706954.1:c.752G>T
ENST00000706955.1:c.*787G>T
ENST00000686459.1:c.*338G>T
ENST00000688158.1:c.*863G>T
ENST00000688308.1:c.752G>T
ENST00000688922.1:c.673G>T
ENST00000693560.1:c.1271G>T
ENST00000371953.8:c.752G>T
ENST00000371953.7:c.752G>T
ENST00000472832.2:c.179G>T
NM_000314.5:c.752G>T
NM_000314.6:c.752G>T
NM_001304717.2:c.1271G>T
NM_001304718.1:c.161G>T
NM_000314.7:c.752G>T
NM_001304717.5:c.1271G>T
NM_001304718.2:c.161G>T

Likely Pathogenic

Met criteria codes 6

PM2_Supporting PS4_Supporting PS2 PP1 PP2 PP3

Not Met criteria codes 2

PS1 PS3

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.752G>T (p.Gly251Val) 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). PS2: De novo (both maternity and paternity confirmed) observation in a patient with the disease and no family history. (internal laboratory contributor(s) ClinVar submitter ID 26957). PP3: REVEL score > 0.7 (score of this variant = 0.968). 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. PP1: Co-segregation with disease in multiple affected family members, with 3 or 4 meioses observed (internal laboratory contributor(s) SCV002669136.2). PS4_P: Proband(s) with phenotype specificity score of 1-1.5 (internal laboratory contributor(s) SCV002669136.2). PM2_P: Absent in large sequenced populations (PMID 27535533).

Met criteria codes

PM2_Supporting	✔	Absent in gnomAD v2 and v4
PS4_Supporting	✔	Ambry: M child w/ intussusception, large hamartoma, 10 total polyps, macrocephaly (PED score = 5)
PS2	✔	GeneDx: Confirmed de novo case in child (PED score = 4)
PP1	✔	3 meioses. Segregates in family of Ambry proband (pos for variant) used for PS4: Mother in 20s neg w/ no clinical hx; Father in 20s pos (de novo) w/ large head, high BP, colonic polyps, esophageal ca; Brother pos w/ ASD, sig speech delay, large head; Brother pos w/ macrocephaly, dermal melanotyctosis, CAL (x1); GM in 40s neg w/ no clinical hx; Male relative (r/ship unknown) in 50s w/ no clinical hx.
PP2	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	✔	REVEL score (0.968) > 0.7

Not Met criteria codes

PS1		✖	c.752_753delinsTG (p.Gly251Val): Variant with limited evidence
PS3		✖	Mighell et al 2018 (PMID 29706350): Low confidence result

Curation History

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