

Variant: *NM_000156.6(GAMT):c.444_448del (p.Phe149fs)*

Version: 1.0

CA2739276352 [↗](#)

2831012 (ClinVar) [↗](#)

Gene: GAMT ([HGNC:2593](#))

Condition: guanidinoacetate methyltransferase deficiency ([MONDO:0012999](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 575ae5db-296a-4eca-9373-1a96016353b9

Approved on: 2026/4/24

Published on: 2026/5/13

HGVS expressions

NM_000156.6:c.444_448del

NM_000156.6(GAMT):c.444_448del (p.Phe149fs)

NC_000019.10:g.1399141_1399145del

CM000681.2:g.1399141_1399145del

NC_000019.9:g.1399140_1399144del

CM000681.1:g.1399140_1399144del

NC_000019.8:g.1350140_1350144del

NG_009785.1:g.7411_7415del

ENST00000252288.8:c.444_448del

ENST00000447102.8:c.444_448del

ENST00000591788.3:c.127_131del

ENST00000640164.1:n.277_281del

ENST00000640762.1:c.375_379del

ENST00000252288.6:c.444_448del

ENST00000447102.7:c.444_448del

ENST00000591788.2:c.129_133del

NM_000156.5:c.444_448del

NM_138924.2:c.444_448del

NM_138924.3:c.444_448del

Likely Pathogenic

Met criteria codes **4**

PVS1_Strong

PP4

PM3

PM2_Supporting

Evidence Links **0**

Expert Panel

Cerebral Creatine Deficiency Syndromes VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** *ClinGen Cerebral Creatine Deficiency Syndromes Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GAMT Version 2.0.0*

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Cerebral Creatine Deficiency Syndromes VCEP

The NM_000156.6:c.444_448del (p.Phe149LeufsTer40) variant in GAMT is a frameshift variant that is predicted to cause a premature stop codon in the last 50 nucleotides of the penultimate exon of the gene and therefore to escape nonsense mediated decay. About 20% of the protein is predicted to be removed (PVS1_Strong). The variant is absent in gnomAD v4.1.0. (PM2_Supporting). One patient with clinical symptoms consistent with GAMT deficiency has been reported with elevated guanidinoacetate and low creatine in dried blood spot, and improvement in seizure frequency after 3 years of creatine treatment (PMID: 35588794) (PP4). This individual is compound heterozygous for the variant and another variant in GAMT that has been classified as likely pathogenic for GAMT deficiency by the CCDS VCEP, c.520T>C (p.Trp174Arg) (ClinVar Variation ID: 1420866), confirmed in trans by parental DNA testing (PMID: 35588794),1 point. (PM3). There is a ClinVar entry for this variant (Variation ID: 2831012). In summary, this variant meets the criteria to be classified as likely pathogenic for guanidinoacetate methyltransferase deficiency. GAMT-specific ACMG/AMP criteria applied, as specified by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel (Specification Version 2.0.0.): PVS1_Strong, PM3, PP4, PM2_Supporting (Classification approved by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel on April 24, 2026)

Met criteria codes

PVS1_Strong			The NM_000156.6:c.444_448del (p.Phe149LeufsTer40) variant in GAMT is a frameshift variant that is predicted to cause a premature stop codon in the last 50 nucleotides of the penultimate exon of the gene and therefore to escape nonsense mediated decay. About 20% of the protein is predicted to be removed (PVS1_Strong).
PP4			One patient with clinical symptoms consistent with GAMT deficiency has been reported with elevated guanidinoacetate and low creatine in dried blood spot, and improvement in seizure frequency after 3 years of creatine treatment (PMID: 35588794) (PP4).
PM3			One patient is compound heterozygous for the variant and another variant in GAMT that has been classified as likely pathogenic for GAMT deficiency by the CCDS VCEP, c.520T>C (p.Trp174Arg) (ClinVar Variation ID: 1420866), confirmed in trans by parental DNA testing (PMID: 35588794). 1 point. (PM3)
PM2_Supporting			The variant is absent in gnomAD v4.1.0. (PM2_Supporting)

Curation History







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