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_002055.5(GFAP):c.1112A>T (p.Glu371Val)

Version: 1.0

CA217117

66438 (ClinVar)

Gene: GFAP (HGNC:2670)
Condition: Alexander disease (MONDO:0008752)
Inheritance Mode: Autosomal dominant inheritance
UUID: 6b60d4d2-3136-4dba-90b7-d0e0849c2c37
Approved on: Fri, 23 Oct 2026 00:00:00 +0000
Published on: Fri, 23 Oct 2026 00:00:00 +0000

HGVS expressions

NM_002055.5:c.1112A>T
NM_002055.5(GFAP):c.1112A>T (p.Glu371Val)
NC_000017.11:g.44911251T>A
CM000679.2:g.44911251T>A
NC_000017.10:g.42988619T>A
CM000679.1:g.42988619T>A
NC_000017.9:g.40344145T>A
NG_008401.1:g.9296A>T
ENST00000253408.11:c.1112A>T
ENST00000435360.8:c.1112A>T
ENST00000253408.10:c.1112A>T
ENST00000435360.7:c.1112A>T
ENST00000585543.6:n.265A>T
ENST00000586125.2:c.47A>T
ENST00000586127.6:n.1641A>T
ENST00000586793.6:c.977A>T
ENST00000587997.6:n.588A>T
ENST00000588735.3:c.1112A>T
ENST00000591327.2:n.2266A>T
ENST00000591880.2:c.42A>T
ENST00000592320.6:c.689A>T
ENST00000638281.1:c.1112A>T
ENST00000638304.1:c.31A>T
ENST00000638488.1:n.53A>T
ENST00000638618.1:c.767A>T
ENST00000639042.1:c.49A>T
ENST00000639277.1:c.1112A>T
ENST00000639921.1:c.69A>T
ENST00000640552.1:n.1126A>T
ENST00000253408.9:c.1112A>T
ENST00000435360.6:c.1112A>T
ENST00000585543.5:n.265A>T
ENST00000586793.5:c.1112A>T
ENST00000588640.5:n.492A>T
ENST00000588735.1:c.83-3135A>T
ENST00000592320.5:c.689A>T
NM_001131019.2:c.1112A>T

NM_001242376.1:c.1112A>T
NM_002055.4:c.1112A>T
NM_001363846.1:c.1112A>T
NM_001131019.3:c.1112A>T
NM_001242376.2:c.1112A>T
NM_001242376.3:c.1112A>T
NM_001363846.2:c.1112A>T

Likely Pathogenic

Met criteria codes 4

PS4_Supporting PM6 PM5 PM2_Supporting

Not Met criteria codes 5

PP4 PM1 PS1 PS2 PS3

Evidence Links 0

Expert Panel

Leukodystrophy and Leukoencephalopathy VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Leukodystrophy and Leukoencephalopathy VCEP

The c.1112A>T variant in GFAP is a missense variant predicted to cause substitution of glutamic acid by valine at amino acid 371 (p.Glu371Val).This variant has been reported as a de novo occurrence with unconfirmed parental relationships in one proband meeting probable diagnosis of Alexander Disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PS4_Supporting, PM6; PMID 21917775). One missense variant, c.1111G>A, p.Glu371Lys (ClinVar Variation ID 1199219), in the same codon has been classified as pathogenic/likely pathogenic for Alexander disease by the ClinGen Leukodystrophy and Leukoencephalopathy VCEP. This variant is absent from gnomAD v4.1.0 (PM2_Supporting). In summary, this variant meets the criteria to be classified as a likely pathogenic variant for Alexander disease based on the ACMG/AMP criteria applied, as specified by the ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0): PS4_supporting, PM6, PM5, PM2_supporting.

Met criteria codes

PS4_Supporting	✔	This variant has been reported in one proband meeting “probable” diagnosis of Alexander Disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PS4_Supporting; PMID 21917775).
PM6	✔	This variant has been identified as a de novo occurrence with unconfirmed parental relationships in one individual with a “probable” diagnosis of Alexander Disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PM6); PMID 21917775).
PM5	✔	One missense variant, c.1111G>A, p.Glu371Lys (ClinVar Variation ID 1199219), in the same codon has been classified as pathogenic/likely pathogenic for Alexander disease by the ClinGen Leukodystrophy and

Leukoencephalopathy VCEP.

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Not Met criteria codes

PP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1	✖	This variant does not reside within a region of amino acids 59-88 that is defined as a mutational hotspot or critical functional domain by the ClinGen Leukodystrophy and Leukoencephalopathy VCEP.
PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	✖	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

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_002055.5(GFAP):c.1112A>T (p.Glu…	Likely Pathogenic	Alexander Disease	2026-10-23	1.0	ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0	GFAP

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