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_000152.4(GAA):c.736delC (p.Leu246Phefs)

Version: 2.2

CA10606113

288505 (ClinVar)

Gene: GAA (HGNC:2548)
Condition: glycogen storage disease II (MONDO:0009290)
Inheritance Mode: Autosomal recessive inheritance
UUID: f22bc2fc-2e19-409d-85f3-342a1122c915
Approved on: 2026/7/6
Published on: 2026/7/6

HGVS expressions

NM_000152.4(GAA):c.736delC (p.Leu246Phefs)
NC_000017.11:g.80107600del
CM000679.2:g.80107600del
NC_000017.10:g.78081399del
CM000679.1:g.78081399del
NC_000017.9:g.75695994del
NG_009822.1:g.11045del
ENST00000570803.6:c.736del
ENST00000572080.2:c.736del
ENST00000577106.6:c.736del
ENST00000302262.8:c.736del
ENST00000302262.7:c.736del
ENST00000390015.7:c.736del
ENST00000570803.5:c.736del
NM_000152.3:c.736del
NM_001079803.1:c.736del
NM_001079804.1:c.736del
NM_000152.4:c.736del
NM_001079803.2:c.736del
NM_001079804.2:c.736del
NM_000152.5:c.736del
NM_001079803.3:c.736del
NM_001079804.3:c.736del

Likely Pathogenic

Met criteria codes 2
PVS1 PM2_Supporting

Not Met criteria codes 1
PM3

Evidence Links 0

Expert Panel
Lysosomal Diseases VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Lysosomal Storage Disorders Variant Curation Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2*
PDF
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000152.5:c.736del (p.Leu246PhefsTer22) variant in GAA is a frameshift variant predicted to cause a premature stop codon in exon 4 out of a total of 20 exons, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). The variant is absent in gnomAD v4.1.0. (PM2_Supporting). One patient with limb girdle muscular dystrophy was reported to be compound heterozygous for c.736delC and another variant in GAA that has been classified by the ClinGen LD VCEP as pathogenic, c.546G>A; the phase is unknown. However, because no additional information is available to support the diagnosis of Pompe disease, such as GAA deficiency, there is insufficient evidence to apply PM3 at this time. There is a ClinVar entry for this variant (Variation ID: 288505. In summary, this variant meets the criteria to be classified as likely pathogenic for Pompe disease. GAA-specific ACMG/AMP criteria applied, as specified by the ClinGen LSD VCEP Specifications Version 2.0): PVS1, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases VCEP on July 6, 2026).

Met criteria codes

PVS1	✔	The NM_000152.5:c.736del (p.Leu246PhefsTer22) variant in GAA is a frameshift variant predicted to cause a premature stop codon in exon 4 out of a total of 20, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting	✔	This variant is absent in gnomAD v4.1.0. (PM2_Supporting).

Not Met criteria codes

PM3	✖	One patient with limb girdle muscular dystrophy was reported to be compound heterozygous for c.736delC and another variant in GAA that has been classified by the ClinGen LD VCEP as pathogenic, c.546G>A; the phase is unknown. However, because no aditional information is available to support the diagnosis of Pompe disease, such as GAA deficiency, there is insufficient evidence to apply PM3 at this time.

Curation History

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