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_000133.3(F9):c.1324G>A (p.Gly442Arg)

Version: 1.1

CA255418

10624 (ClinVar)

Gene: F9 (HGNC:2158)
Condition: hemophilia B (MONDO:0010604)
Inheritance Mode: X-linked inheritance
UUID: 02950049-a7cc-452b-a511-516a83f85670
Approved on: 2025/3/10
Published on: 2025/3/28

HGVS expressions

NM_000133.3(F9):c.1324G>A (p.Gly442Arg)
NM_000133.3:c.1324G>A
NC_000023.11:g.139562009G>A
CM000685.2:g.139562009G>A
NC_000023.10:g.138644168G>A
CM000685.1:g.138644168G>A
NC_000023.9:g.138471834G>A
NG_007994.1:g.36274G>A
ENST00000218099.7:c.1324G>A
ENST00000643157.1:n.1723+268G>A
ENST00000218099.6:c.1324G>A
ENST00000394090.2:c.1210G>A
NM_001313913.1:c.1210G>A
NM_000133.4:c.1324G>A
NM_001313913.2:c.1210G>A

Pathogenic

Met criteria codes 3

PP3 PS4_Very Strong PM2_Supporting

Not Met criteria codes 2

PP4 PM5

Evidence Links 0

Expert Panel

Coagulation Factor Deficiency VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Coagulation Factor Deficiency Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for F9 Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Coagulation Factor Deficiency VCEP

The c.1324G>A (NM_000133.4) variant in F9 is a missense variant predicted to cause substitution of Glycine by Arginine at amino acid 442 (p.Gly442Arg). This variant has been reported in at least 8 probands with severe or moderate hemophilia B (PS4_Very Strong; PMID: 24656159, 27109384, 22544209, 29296726, 8055323, 10739381, 2714791). This variant is absent from gnomAD v2.1, v3.1.2. The

computational predictor REVEL gives a score of 0.933, which is above the threshold of 0.6, evidence that correlates with impact to F9 function (PP3). In summary, this variant meets the criteria to be classified as pathogenic for X-linked recessive hemophilia B based on the ACMG/AMP criteria applied, as specified by the ClinGen Coagulation Factor Deficiency VCEP for F9: PS4_Very Strong, PP3, PM2_Supporting.

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.933, which is above the threshold of 0.6, evidence that correlates with impact to F9 function (PP3). SpliceAI predicts no impact on splicing with a delta score of 0.
PS4_Very Strong	✔	This variant has been reported in at least 8 probands meeting the hemophilia B phenotype criteria specified by the Coagulation Factor Deficiency VCEP (PS4_VeryStrong; PMID: 24656159, 27109384, 22544209, 29296726, 8055323, 10739381, 2714791).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1 and v3.1.2.

Not Met criteria codes

PP4	✖	There is one MLOF proband. However, this proband can be used for PS4 to reach the Very Strong strength. Not applying PP4_Moderate.
PM5	✖	Although 3 other variants at the same residue are seen, Gly442Glu, Gly442Ala and Gly442Val, this variant does not need PM5 to reach Pathogenic.

Curation History

Showing 1 to 2 of 2 rows

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