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_000133.4(F9):c.224G>A (p.Arg75Gln)

Version: 1.0

CA255318

10573 (ClinVar)

Gene: F9 (HGNC:2158)
Condition: hemophilia B (MONDO:0010604)
Inheritance Mode: X-linked inheritance
UUID: 178efdc9-7922-4e7d-8479-352a42eedd02
Approved on: 2024/10/11
Published on: 2025/1/7

HGVS expressions

NM_000133.4:c.224G>A
NM_000133.4(F9):c.224G>A (p.Arg75Gln)
NC_000023.11:g.139537145G>A
CM000685.2:g.139537145G>A
NC_000023.10:g.138619304G>A
CM000685.1:g.138619304G>A
NC_000023.9:g.138446970G>A
NG_007994.1:g.11410G>A
ENST00000218099.7:c.224G>A
ENST00000218099.6:c.224G>A
ENST00000394090.2:c.224G>A
ENST00000479617.2:n.231G>A
NM_000133.3:c.224G>A
NM_001313913.1:c.224G>A
NM_001313913.2:c.224G>A

Pathogenic

Met criteria codes 4

PM2_Supporting PP3 PS4_Very Strong PP4_Moderate

Not Met criteria codes 1

PM1

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

NM_000133.4(F9):c.224G>A (p.Arg75Gln) missense variant has a REVEL score of 0.904, which meets criteria for PP3. This variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3). Approximately 24 patients are reported in the literature with mild hemophilia B and this variant, meeting F9 phenotype criteria for PS4_Very strong (PMID: 31064749, PMID: 2066105, PMID: 8314564, PMID:

29296726, PMID: 27213901, PMID: 2773937). In summary, this variant meets criteria to be classified as pathogenic. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel for F9: PS4_Very strong, PP4_Moderate, PP3, PM2_supporting.

Met criteria codes

PM2_Supporting	✔	This variant is absent from males in population databases (gnomAD v2.1.1/gnomAD v3).
PP3	✔	REVEL score is 0.904, which is below the 0.6 cutoff.
PS4_Very Strong	✔	Greater than 16 individuals reported in the literature with mild hemophilia B. The criterion is met at the very strong evidence level.
PP4_Moderate	✔	Counting one of the MLOF probands

Not Met criteria codes

PM1	✖	Variant is not within exons 3, 4 or 5.

Curation History

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