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Variant: NM_000133.4(F9):c.277G>A (p.Asp93Asn)

Version: 1.0

CA414436678

994410 (ClinVar)

Gene: F9 (HGNC:2158)
Condition: hemophilia B (MONDO:0010604)
Inheritance Mode: X-linked inheritance
UUID: ee4724ea-b5b0-4913-ac8e-dc8baa922b48
Approved on: 2025/5/2
Published on: 2025/5/2

HGVS expressions

NM_000133.4(F9):c.277G>A (p.Asp93Asn)
NM_000133.4:c.277G>A
NC_000023.11:g.139537386G>A
CM000685.2:g.139537386G>A
NC_000023.10:g.138619545G>A
CM000685.1:g.138619545G>A
NC_000023.9:g.138447211G>A
NG_007994.1:g.11651G>A
ENST00000218099.7:c.277G>A
ENST00000218099.6:c.277G>A
ENST00000394090.2:c.277G>A
ENST00000479617.2:n.241+231G>A
NM_000133.3:c.277G>A
NM_001313913.1:c.277G>A
NM_001313913.2:c.277G>A

Pathogenic

Met criteria codes 3

PP3 PS4_Very Strong PM2_Supporting

Not Met criteria codes 2

PM1 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 F8 Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Coagulation Factor Deficiency VCEP

The NM_000133.4(F9):c.277G>A (p.Asp93Asn) variant is completely absent from gnomAD v2.1.1 and v3.1.2 meeting PM2_Supporting. At least 8 individuals with moderate-severe hemophilia B are found in the literature (PMIDs: 29296726, 11013449, 8091381, 22103590, 10698280, 2198809, 24656159) meeting criteria for PS4_Very strong. This missense variant has a REVEL score of 0.754 (>0.6), and the

nucleotide is the last in exon 3 which SpliceAI predicts results in the loss of the splice donor of intron 3 (delta score of 0.93) meeting PP3. 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, PP3, PM2_Supporting.

Met criteria codes

PP3	✔	The c.277G>A (p.Asp93Asn) missense variant has a REVEL score of 0.754 (>0.6). The nucleotide is the last in exon 3 and SpliceAI predicts that this variant results in the loss of the splice donor of intron 3 (delta score of 0.93).
PS4_Very Strong	✔	At least 8 individuals with moderate-severe hemophilia B are found in the literature meeting criteria for PS4. All known cases were used for PS4 to maximize use at very strong (8 points).
PM2_Supporting	✔	The c.277G>A (p.Asp93Asn) variant is completely absent from gnomAD v2.1.1 and v3.1.2.

Not Met criteria codes

PM1	✖	The variant occurs in the last nucleotide of exon 3; however, this variant is predicted to cause a splicing defect, so this code is not applied.
PM5	✖	Four variants at the same residue, Asp93His, Asp93Gly, Asp93Val, and Asp93Glu have been reported; however, this variant is suspected to cause a splicing defect so these additional variants were not evaluated.

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000133.4(F9):c.277G>A (p.Asp93A...	Pathogenic	Hemophilia B	2025-05-02	1.0	ClinGen Coagulation Factor Deficiency Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for F8 Version 1.0.0	F9

Showing 1 to 1 of 1 rows

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