

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 



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