

Variant: *NM_000132.4(F8):c.984T>G (p.Phe328Leu)*

Version: 1.0

CA414917660 [↗](#)

666959 (ClinVar) [↗](#)

Gene: F8 ([HGNC:2157](#))

Condition: hemophilia A ([MONDO:0010602](#))

Inheritance Mode: X-linked inheritance

UUID: 15ff0731-58a6-4dcc-a376-7c7420af226d

Approved on: 2026/5/1

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HGVS expressions

NM_000132.4(F8):c.984T>G (p.Phe328Leu)

NM_000132.4:c.984T>G

NC_000023.11:g.154969356A>C

CM000685.2:g.154969356A>C

NC_000023.10:g.154197631A>C

CM000685.1:g.154197631A>C

NC_000023.9:g.153850825A>C

NG_011403.1:g.58368T>G

NG_011403.2:g.58368T>G

ENST00000360256.9:c.984T>G

ENST00000647125.1:c.*860T>G

ENST00000360256.8:c.984T>G

NM_000132.3:c.984T>G

Likely Pathogenic

Met criteria codes **4**

PM2_Supporting

PP4_Moderate

PS4

PP3

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 2.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Coagulation Factor Deficiency VCEP

The NM_000132.4(F8):c.984T>G; p.Phe328Leu variant is a missense variant in F8 gene. This variant is absent in males in gnomAD v4.1.0 (PM2_Supporting) and is predicted to have a deleterious effect (REVEL score of 0.824; PP3), which is greater than the threshold for PP3 (>0.6). This variant has been observed in at least 5 patients in the literature (PMID:25550078, 2 points PS4; PMID:18691168, 1 point PS4; PMID:23711294, 1 point PS4; PMID:29296726, 2 points PP4; PP4_Moderate) and 2 patients from an internal laboratory cohort with mild hemophilia A with type 2N von Willebrand disease ruled out (2 points PS4, total 5 points PS4, PS4). In summary, this variant meets the

criteria to be classified as likely pathogenic for hemophilia A. ACMG/AMP criteria applied, as specified by the Coagulation Factor Deficiency Variant Curation Expert Panel (specifications version 2.0.0) for F8: PS4, PP4_Moderate, PM2_Supporting, PP3.

Met criteria codes

PM2_Supporting			This variant is absent in males in gnomAD v4.1.0 (PM2_Supporting).
PP4_Moderate			There is at least 1 proband with mild hemophilia A without confirmed exclusion of type 2N von Willebrand disease (PMID:29296726, 2 points PP4; PP4_Moderate).
PS4			This variant has been observed in at least 4 patients in the literature (PMID:25550078, 2 points PS4; PMID:18691168, 1 point PS4; PMID:29296726; PMID:23711294, 1 point PS4) and 2 patients from an internal laboratory cohort with mild hemophilia A with type 2N von Willebrand disease ruled out (2 points PS4, total 6 points PS4).
PP3			This variant is predicted to have a deleterious effect (REVEL score of 0.824; PP3), which is greater than the Clingen CFD threshold for PP3 (>0.6), with splicing predicted to be unaffected (SpliceAI scores less than 0.1).

Curation History

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