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# *Variant: NM_000132.4(F8):c.6976C>T (p.Arg2326Ter)*

Version: 1.1

*CA255007*

*10085 (ClinVar)*

**Gene**: F8 (HGNC:2157)
**Condition**: hemophilia A (MONDO:0010602)
**Inheritance Mode**: X-linked inheritance
**UUID:** 4e8e0239-4155-44c7-b22f-2aea4ebb9066
**Approved on**: 2026/1/26
**Published on**: 2026/1/26

## *HGVS expressions*

**NM_000132.4(F8):c.6976C>T (p.Arg2326Ter)**
**NM_000132.4:c.6976C>T**
NC_000023.11:g.154837677G>A
CM000685.2:g.154837677G>A
NC_000023.10:g.154065952G>A
CM000685.1:g.154065952G>A
NC_000023.9:g.153719146G>A
NG_011403.1:g.190047C>T
NG_033065.1:g.1986C>T
NG_011403.2:g.190047C>T
ENST00000360256.9:c.6976C>T
ENST00000644698.1:c.709C>T
ENST00000330287.10:c.571C>T
ENST00000360256.8:c.6976C>T
NM_000132.3:c.6976C>T
NM_019863.2:c.571C>T
NM_019863.3:c.571C>T

**Pathogenic**

**Met criteria codes** 6

PP4_Moderate PS2_Moderate PS4_Very Strong PM2_Supporting PP1 PVS1_Strong

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 c.6976C>T (p.Arg2326Ter) creates a premature stop codon in exon 26, which is the last exon of the F8 gene. Therefore, protein is not expected to undergo NMD and meets PVS1_Strong. This variant is completely absent from gnomAD v2.1.1 and v3.1.1, which meets PM2_Supporting. More than 20 patients are reported in the literature with severe/moderate hemophilia A, meeting F8 phenotype criteria for PS4_Very strong and PP4_Moderate. The variant was also reported in two affected brothers and their carrier mother, which meets criteria for PP1 (PMID: 2987704). There is also at least one report of a de novo case where maternity was not confirmed, meeting PS2_Moderate (PMID: 2104741). 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: PVS1_Strong, PS4_Very strong, PS2_Moderate, PP4_Moderate, PM2_Supporting, PP1.**

**Met criteria codes**

| | | |
|---|---|---|
| **PP4_Moderate** | ✔ | Counting one MLOF proband |
| **PS2_Moderate** | ✔ | 1 severe hemophilia A patient with de novo variant; maternity not confirmed. |
| **PS4_Very Strong** | ✔ | Variant has been report in more than 20 individuals in the literature with severe/moderate hemophilia A. Therefore, criteria for PS4_Very strong is met. |
| **PM2_Supporting** | ✔ | Variant is absent in males in gnomAD v.2.1.1 and v3.1. |
| **PP1** | ✔ | Variant identified in two affected brothers and their mother (2 meioses). |
| **PVS1_Strong** | ✔ | Variant causes an in frame stop that is not expected to undergo NMD. |

Curation History

Showing 1 to 2 of 2 rows

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