

Variant: *NM\_019863.3:c.347T>C*

Version: 1.0

CA10567758 [↗](#)

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

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

**Inheritance Mode:** X-linked inheritance

**UUID:** 0a48c03f-d7c4-45f4-a631-e37c1c45edf2

**Approved on:** 2026/4/10

**Published on:** 2026/4/12

### *HGVS expressions*

**NM\_019863.3:c.347T>C**

NC\_000023.11:g.154860580A>G

CM000685.2:g.154860580A>G

NC\_000023.10:g.154088855A>G

CM000685.1:g.154088855A>G

NC\_000023.9:g.153742049A>G

NG\_011403.1:g.167144T>C

NG\_011403.2:g.167144T>C

ENST00000360256.9:c.6752T>C

ENST00000644698.1:c.485T>C

ENST00000330287.10:c.347T>C

ENST00000360256.8:c.6752T>C

NM\_000132.3:c.6752T>C

NM\_019863.2:c.347T>C

NM\_000132.4:c.6752T>C

**Pathogenic**

**Met criteria codes** **3**

PP3

PS4\_Very Strong

PM2\_Supporting

**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.6752T>C (p.Val2251Ala) is a missense variant in F8 that is absent from from gnomAD v4.1.0 meeting PM2\_Supporting. The variant is predicted to have a deleterious effect with a REVEL score of 0.953 meeting PP3. The variant has been observed in at least eight probands in the literature and one proband in an internal laboratory cohort with mild to moderate hemophilia A,

both with and without inhibitors meeting PS4\_Very\_Strong (PMID:41071185, 24553597, 23926300, 20331761, 10910913, internal laboratory cohort). In summary, this variant meets the criteria to be classified as 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\_Very\_Strong, PM2\_Supporting, PP3.

Met criteria codes

|                 |                                                                                   |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|-----------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PP3             |  |  | This variant is predicted to have a deleterious effect (REVEL score of 0.953; 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).                                                                                                                                                                                                   |
| PS4_Very Strong |  |  | This variant has been observed in at least eight probands in the literature and one proband in an internal laboratory cohort with mild to moderate hemophilia A, both with and without inhibitors (PMID:41071185, 3 points PS4; PMID:24553597, 1 point PS4; PMID:23926300, 2 points PS4; PMID:20331761, 1 point PS4; PMID:10910913, 1 point PS4; internal laboratory cohort, 1 point PS4; Total 9 points PS4, PS4_Very_Strong). |
| PM2_Supporting  |  |  | This variant is absent from gnomAD v4.1.0 (PM2_Supporting).                                                                                                                                                                                                                                                                                                                                                                     |

Curation History 

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